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CHEMICAL SPECIALTIES MANUFACTURERS ASSOCIATION

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Product Ingredient
Review Program

ORIGINAL

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August 24, 1993

Not for CBI

Dr. John Walker
Executive Director
ITC (TS-792)
Washington, DC 20460



84940000022

Dear John:

The Chemical Specialties Manufacturers Association (CSMA) on behalf of the Fabric Softener Quats Steering Committee (QSC) is responding to the ITC's February 22, 1993, letter requesting additional information on Imidazolium Quaternary Ammonium Compounds (IQAC) and Ethoxylated Quaternary Ammonium Compounds (EQAC). The QSC participants are, Croda, Inc., Stepan Company, and Witco Corporation.

Enclosed you will find five (5) copies of a July 29, 1993 compilation of additional information and responses in regard to data submissions from FSQ Steering Committee members filed in response to the 22nd Report of the TSCA Interagency Testing Committee.

Information contained in these studies should not be reviewed, abstracted, or used by persons other than EPA without the expressed written consent of the Fabric Softener Quats Joint Venture/Chemical Specialties Manufacturers Association except as required to carry out the requirements of TSCA.

If you have questions, please contact Jim T. Hill, Ph.D., Director, Product Ingredient Review Program, CSMA, at 202-872-8110.

Sincerely,

Ralph Engel, Pres.

Ralph Engel -
President, CSMA
for the Fabric Softener Quats
Steering Committee

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enclosures

cc: FSQ Steering Committee

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Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

An Expert Report Prepared for:

Fabric Softener QUATS Steering Committee

c/o CSMA PIR Program

Report Prepared by:

John A. Todhunter, Ph.D.
Fellow, American Institute of Chemists
Diplomate, American Board of Toxicology

Date:

July 29, 1993

TEXT OF RESPONSES TO QUESTIONS IN INTERAGENCY TESTING
COMMITTEE LETTER OF FEBRUARY 22, 1993

In Regard to the Studies Cited in a January 17, 1984 Cover Letter from Howard Hickman, Sherex Chemical Co. -

IQAC (CAS No. 68122-86-1):

1. Two acute oral toxicity studies in rats were noted in the cover letter, but only one study of this type was found by ITC and it was for CAS No. 68413-04-7, a PEQ analog.

Additional copies of the acute oral toxicity studies on CAS No. 68122-86-1 are provided along with this response [See Attachments 1 & 2].

2. One eye irritation study in rabbits was listed in the cover letter; two studies of this type were found but were for PEQ analogs CAS No. 68413-04-7 and CAS No. 68389-89-9.

The eye irritation studies (additional copies provided as Attachments 2 & 3) contain information specific to IQAC 68122-86-1 at pages 2 and 29 of Attachment 2 and the full text of Attachment 3. Other QUATS are noted as well in these studies.

3. One skin irritation study in rabbits was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS NO. 68413-04-7 and CAS No. 68389-89-9.

The skin irritation studies (additional copies provided as Attachments 2, 4 & 5) contain information specific to IQAC 68122-86-1 at page 21 of Attachment 2 and the full text of Attachments 4 & 5. Other QUATS are noted as well in these studies.

4. One dermal sensitization study in Guinea pigs was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS NO. 68413-04-7 and CAS No. 68389-89-9.

The skin sensitization studies (additional copies provided as Attachment 6) contain information specific to IQAC 68122-86-1. Other QUATS may be noted as well in these studies.

5. One biodegradation study was listed in the cover letter, but it is unclear if the submitted study is for IQAC or for an analog of IQAC.

The biodegradation study (additional copy provided, Attachment 7) contains information specific to IQAC 68122-86-1.

PEQ (CAS No. 68410-69-5):

1. One rat acute oral toxicity study was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The acute oral toxicity studies (additional copies provided as Attachments 8, 9, 10, 11 & 12) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

2. One eye irritation study in rabbits was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The eye irritation studies (additional copies provided as Attachments 8, 9, 10, 11, 13, & 14) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

3. One skin irritation study in rabbits was listed in the cover letter; two studies of this type were submitted, but were for PEQ analogs CAS No. 68389-89-9 and CAS No. 68413-04-7.

The skin irritation studies (additional copies provided as Attachments 8, 9, 10, 11, 15, 16 & 17) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

4. One skin sensitization study in rabbits was listed in the cover letter; one study of this type was submitted, but was for PEQ analog CAS No. 68389-89-9.

The skin sensitization studies (additional copies provided as Attachments 18, 19, and 20) contain information specific to PEQ 68410-69-5. Other QUATS may be noted as well in these studies.

5. One biodegradation study was listed in the cover letter, but it is unclear if the submitted study is for PEQ or an analog of PEQ.

The biodegradation study (additional copy provided, Attachment 21) contains information specific to PEQ 68410-69-5.

In Regard to the Studies Cited in Procter & Gamble 1984a and/or Procter and Gamble 1988 Cover Letters -

IQAC (CAS No. 68122-86-1):

1. One oral absorption, distribution, and metabolism study in rats was listed in the cover letter; one study of this type was submitted for an IQAC analog (structurally different than IQAC) CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the metabolism of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the absorption, fate, distribution, and metabolism of 72623-82-6 from oral administration in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

In both cases, initial hydrolysis in the stomach will remove the fatty amido groups from the (2-fatty amido)ethyl group attached to the No. 1 nitrogen of the imidazolium ring. This will generate a fatty acid residue which differs between the two compounds only in the range of the carbon chain length. The imidazolium function itself will remain quaternized and retain its bulky long chain alkyl moiety at the No. 2 position of the ring. Clearly, this imidazolium residue's absorption will be dictated by its charge and molecular volume: in the stomach, absorption will be poor to non-significant due to the cationic charge. In the intestine it will be charged to a lesser degree but will be expected to complex with bile salts and be excreted in the feces. This is exactly what is observed for 72623-82-6 and there is no reasonable scientific basis to conclude that 68122-86-1 will behave any differently. Indeed, as discussed, there are ample scientific bases to conclude that 68122-86-1 will exhibit ADME behavior essentially identical to that of 72623-82-6.

2. One dermal absorption, distribution, and metabolism study in rats was listed in the cover letter; one study of this type was submitted for IQAC analog with CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the metabolism of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the absorption, fate, distribution, and metabolism of 72623-82-6 from dermal application in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

In both cases, dermal absorption will be poor due to the cationic charge and the molecular size. It is well established that ionic substances are poorly absorbed from the skin and, also, that increasing molecular volume decreases the rate of skin absorption for homologous compounds. There is no mechanism available on the skin for destruction of the charged nature of the imidazolium group and, therefore, no mechanism to overcome this significant bar to effective dermal uptake of these substances. Also, at the dermal pH, little hydrolysis of the substances' fatty amido side chains is expected, thus a large molecular mass will be retained. To the extent that any of either substance is absorbed, it will not require metabolism to be excreted (since it would already carry a charge) and - due to the fatty and charged nature of these compounds, biliary excretion can be predicted to predominate all other modes of excretion. This is exactly what is observed for 72623-82-6 and there is no reasonable scientific basis to conclude that 68122-86-1 will behave any differently. Indeed, as discussed, there are ample scientific bases to conclude that 68122-86-1 will exhibit ADME behavior essentially identical to that of 72623-82-6.

3. One mouse lymphoma study was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the mutagenicity of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the mutagenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

As can be seen from Figure 1, the only reactive center of any significance in these two compounds is the fatty amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned and which for both compounds would involve essentially the same acyl transfer. Therefore, a gene toxicity test of either one of these substances will be valid as a predictor for the gene toxicity potential of the other.

4. One in vivo cytogenetics study in rats was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the clastogenic potential of CAS No. 68122-86-1 since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the clastogenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Clastogenic effects may occur by direct gene toxicity due to reaction of the clastogen with the genetic material (leading to damage of a sort requiring recombination repair or replacement of large sections of material) or by interference with chromatid separation during mitosis.

The former mechanism would require a reactive center on the compound of interest (either pre-existing or formed by action of the microsomal oxidase system). As can be seen from Figure 1, the only reactive center of any significance in these two compounds is the fatty amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned and which for both compounds would involve essentially the same acyl transfer. Therefore, a clastogenicity test of either one of these substances will be valid as a predictor for the clastogenic potential of the other, if they work by a mechanism involving reaction with genetic material.

The latter mechanism would require interference with cytoskeletal functions, which could - conceivably - be produced by membrane active substances. These would, however, be physical-chemical effects involving membrane solubility which, for both 68122-86-1 and 72632-82-6 will be the same based on the near identity of physical-chemical properties affecting lipid and water solubility. Therefore, a clastogenicity test of either one of these substances will be valid as a predictor for the clastogenic potential of the other, if they work by a mechanism involving interference with cytoskeletal function.

5. One teratology study in rats was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to induce developmental and teratogenic effects since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the developmental toxicity / teratogenic potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Neither compound (see discussion above for points Nos. 1 and 2) will be absorbed to any significant degree from the oral or dermal routes or undergo any significant metabolism. Neither substance will have any gene toxicity potential (see discussion for point Nos. 3 and 4, above, and No. 6, below). Therefore, if either substance has any developmental or teratogenic effect it will be produced by: (a) high dose interference with proper maternal nutrition which, since it results from a purely physical-chemical effect on the gastro-intestinal tract, can not differ from one substance to the other; (b) membrane disruption or disruption of cell:cell interaction which, since this type of effect is produced by physico-chemical interaction with cell membranes, can not vary between the two compounds in question; or, (c) alterations of pH or electrolyte balance in the micro-environment of the developing embryo / fetus, either of which, being physico-chemical effects, would be equally produced by either substance. Therefore, teratology studies on 72623-82-6 will be equally predictive for 68122-86-1.

6. One unscheduled DNA synthesis study in human diploid cells was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to induce unscheduled synthesis of DNA since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the general gene damaging potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Unscheduled DNA synthesis occurs as cells try to repair non-specific damage to the genetic material. This, if it is compound related, results from reaction between the genetic material and a reactive center in the compound. The center may be pre-existing in the compound or may be formed by the action of the microsomal

oxidase system. As can be seen from Figure 1, the only reactive center of any significance in these two compounds is the fatty amido group. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the imidazolium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned and which for both compounds would involve essentially the same acyl transfer. Therefore, an unscheduled DNA synthesis test of either one of these substances will be valid as a predictor for the non-specific genetic damage potential of the either.]

7. One bioconcentration study in blugills was listed in the cover letter; one study of this type was submitted for IQAC analog CAS No. 72623-82-6.

This study is considered by the submitter to be appropriate for evaluating the ability of CAS No. 68122-86-1 to bioconcentrate since there are no significant structural differences between 68122-86-1 (see Figure 1) and 72623-82-6 (see Figure 1) which would be expected to affect the bioconcentration potential of 72623-82-6 in comparison to 68122-86-1. The sole difference between 68122-86-1 and 72623-82-6 is that the former is made with soft tallow and the latter is made with hydrogenated tallow as the source of the fatty amido side chains.

Bioconcentration is purely dictated by physico-chemical properties. So long as two substances have essentially identical physico-chemical properties and they are not metabolized in vivo to substances with distinct physico-chemical properties, a study on one will be completely predictive for the other. CAS 68122-86-1 and CAS 72623-82-6 have essentially identical octanol-water partition coefficients, essentially identical water solubilities, and will be identically metabolized (if they are metabolized at all) by loss of the fatty acyl function via hydrolysis of the fatty amido group. Therefore, there can not be any difference in the bioaccumulation potential of 68122-86-1 compared to that of 72632-82-6.

EEQ (CAS No. 68153-35-5)

1. One acute oral toxicity study in the rat was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit acute oral toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no acute oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the acute oral toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute oral toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds have a quaternary center to which are attached two aminoalkyl groups, a methyl group, and a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the aminoalkyl groups). These substances will all be charged, bulky species and, like the IQAC compounds, will not absorb well from the gastro-intestinal tract. The acute oral toxic effects produced will, thus, be due to any gastrointestinal irritation which is produced. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, these substances will all have similar, low, acute oral toxicity and the toxicity of one is predictive of the others.

2. One acute dermal toxicity study in rabbits was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit acute dermal toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no acute oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the acute dermal toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute dermal toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds have a quaternary center to which are attached two aminoalkyl groups, a methyl group, and a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the aminoalkyl groups). These substances will all be charged, bulky species and, like the IQAC compounds, will not absorb well from the skin. The acute dermal toxic effects produced will, thus, be limited to local effects of irritation. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, these substances will all have similar, low, acute dermal toxicity and the toxicity of one is predictive of the others.

3. One eye irritation study in rabbits was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did indeed submit eye irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no eye irritation data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the eye irritation potential of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different eye irritation potential (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case. Since these compounds produce eye irritation by a physico-chemical effect, and since these compounds have similar physico-chemical properties, these substances will all have similar eye irritation potential and a study of one is predictive of the others.

4. One skin irritation study in rabbits was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did indeed provide skin irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no skin irritation data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the skin irritation potential of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see

Figure 2) would not reasonably be expected to produce a different skin irritation potential (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case. Since these compounds produce eye irritation by a physico-chemical effect, and since these compounds have similar physico-chemical properties, these substances will all have similar eye irritation potential and a study of one is predictive of the others.

5. One subchronic toxicity study (route not specified) was listed in the cover letter; a dermal toxicity study was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit subchronic dermal toxicity studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no subchronic oral toxicity data of its own which is specific to EEQ CAS No. 68153-35-5 since EEQ is not manufactured for fabric softener use;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the subchronic dermal toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different acute dermal toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 all three compounds have a quaternary center to which are attached two aminoalkyl groups, a methyl group, and a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the aminoalkyl groups). These substances will all be charged, bulky species and, like the IQAC compounds, will not absorb well from the skin or the gastrointestinal tract. Accordingly, the dermal sub-

chronic toxic effects produced will be limited to local irritation (chemical dermatitis) and the subchronic oral effects will be limited to effects on the gastrointestinal mucosa. Since both sorts of effects are driven by the physico-chemical properties of a substance, and since these compounds have similar physico-chemical properties, these substances will all have similar, low, subchronic (dermal or oral) toxicity potential and a study of one will be predictive of the others.

6. One Ames Salmonella/microsome plate test was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

This study is considered by the submitter to be appropriate for evaluating the mutagenic potential of CAS No. 68153-35-5 since the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not be expected give 68389-89-9 any different mutagenic potential than 68153-35-5, making an Ames test of the PEQ analog an excellent index of mutagenic potential of PEQs in general and of the homologous EEQ as well. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2, the only reactive center of any significance in these two compounds is the fatty amido group and this is essentially identical in both compounds. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the ammonium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned, which for both compounds would involve essentially the same acyl transfer. Therefore, a gene toxicity test of either one of these substances will be valid as a predictor for the gene toxicity potential of the other.

7. One mouse lymphoma study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

This study is considered by the submitter to be appropriate for evaluating the mutagenic potential of CAS No. 68153-35-5 since the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not be expected give 68389-89-9 any different mutagenic potential than 68153-35-5, making a mouse lymphoma test of the PEQ analog an excellent index

of mutagenic potential of PEQs in general and of the homologous EEQ as well. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2, the only reactive center of any significance in these two compounds is the fatty amido group and this is essentially identical in both compounds. This could, conceivably, provide an electrophilic center for attack by a suitable nucleophile with resulting transfer of the fatty acyl group. At intracellular pH's this will require a powerful nucleophile and such reactions, when they occur, are known to occur preferentially to a thiol acceptor (forming a thioester). Due to the charged nature of the ammonium group, binding to the microsomal membranes and service there as a substrate for microsomal oxidases will not be favored and, thus, the only viable mechanism for either substance to react with the genetic material is via the acyl transfer just mentioned, which for both compounds would involve essentially the same acyl transfer. Therefore, a gene toxicity test of either one of these substances will be valid as a predictor for the gene toxicity potential of the other.

8. One human skin irritation study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit human skin irritation studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no human skin irritation studies of its own which are specific to EEQ CAS No. 68153-35-5 since this is not manufactured for fabric softeners;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analogs for which data was provided will accurately predict the skin irritation potential of EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) or 68410-69-5 (see Figure 2) would not reasonably be expected to produce a different potential for skin irritation (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. Since this is a physico-chemical property, and since these compounds have similar physico-chemical properties, these substances will all have similar skin irritation potential and a study of one is predictive of the others. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one

ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

9. One human skin sensitization study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS NO. 68389-89-9 and PEQ CAS No. 68410-69-5.

Procter and Gamble did, indeed, submit human skin sensitization studies on two PEQ compounds. This was done since:

- (a) Procter and Gamble has no human skin sensitization data of its own which is specific to EEQ CAS No. 68153-35-5 since this is not manufactured for fabric softeners;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQs may be taken as reasonable analogs in regard to dermal sensitization potential since the mode of action, if any, would be acylation of protein material by the tallow amido groups found in both EEQ and PEQ (by trans-amidation to protein amino functional groups). Therefore, the analogs provided will give the same sensitization potential as will EEQ. The relevant structures are shown in Figure 2.

10. One acute bluegill toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to bluegill sunfish on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on the bluegill sunfish;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to fish (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy

unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

11. One acute sheepshead minnow toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to sheepshead minnows on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on the sheepshead minnows;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to fish (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an

average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

12. One acute mysid shrimp toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to mysid shrimp on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on mysid shrimp;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different aquatic invertebrate toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These

membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

13. One acute Daphnia magna toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

Procter and Gamble did, indeed, provide data on the aquatic toxicity to Daphnia on a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on Daphnia;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different aquatic invertebrate toxicity (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to aquatic organisms by disrupting sensitive membranes which are required for oxygen and gas exchange between the organism and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to aquatic organisms and a study of one will be predictive of the other.

14. One freshwater algae toxicity study was listed in the cover letter; a study of this type was submitted for PEQ analog CAS No. 68389-89-9.

[Procter and Gamble did indeed provide data on the aquatic toxicity to freshwater algae of a PEQ compound. This was done since:

- (a) Procter and Gamble has no aquatic toxicity data of its own which is specific to the effects of EEQ CAS No. 68153-35-5 on freshwater algae;
- (b) Procter and Gamble wished to provide relevant information; and,
- (c) the PEQ analog for which data was provided will accurately predict the aquatic toxicity of the EEQ.

This is because the structural differences between 68153-35-5 (see Figure 2) and 68389-89-9 (see Figure 2) would not reasonably be expected to produce a different toxicity to algae (in terms of potency or effects) for the PEQ compounds in comparison to EEQ. After all, EEQ is in reality a homolog of PEQ in which the average number of ethoxy units in the polyethoxy chain is less than 1.5. "Pure" EEQ would of course have only one ethoxy unit in the side chain. Thus, a distinction between commercial EEQ and PEQ is somewhat artificial in any case.

As can be seen from Figure 2 both compounds have a quaternary center to which are attached two aminoalkyl group, a hydroxy alkyl group (this is a polyoxyethylene chain with an average number of ethoxyl units greater than 1.5 in the PEQs and with an average number of ethoxyl units of 1.5 or less in EEQ). Each structure also has two tallow amide chains identically attached (to the nitrogen of the amino alkyl groups). These substances will all be charged, bulky species with a strong surfactant/detergent property. Such substances belong to a very broad class of agents which exhibit toxicity to algae by disrupting sensitive membranes which are required for metabolic processes and gas exchange between the algae and the surrounding water. These membrane effects are driven by the physico-chemical properties of detergent / surfactant substances, and since EEQ and the PEQ analog have similar physico-chemical properties, both these substances will all have similar degrees of toxicity to freshwater algae and a study of one will be predictive of the other.

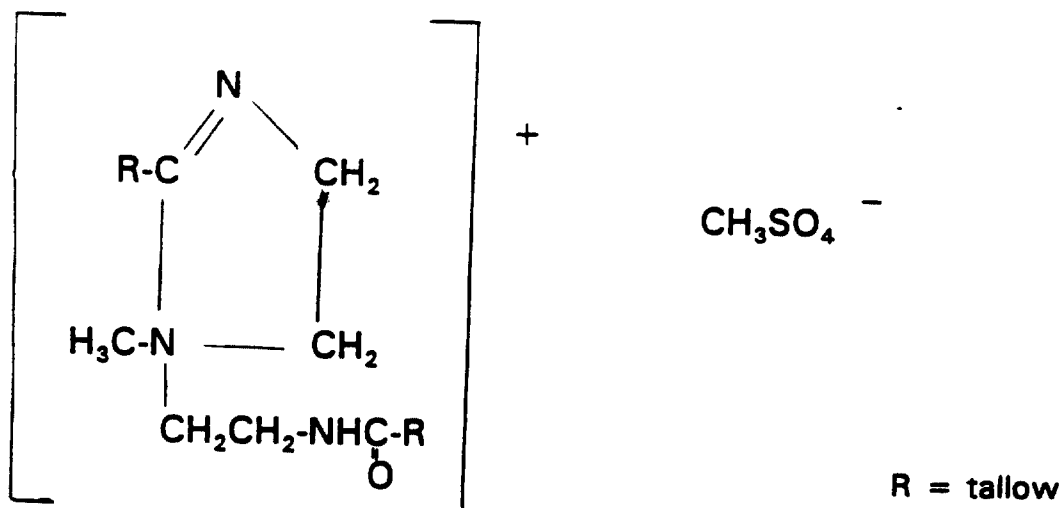
Procter and Gamble Tests on Varisoft 475

The purpose of the referenced 91 day percutaneous toxicity study in rabbits was to examine the toxicity potential of Varisoft 475 (which is 75% to 90% IQAC [CAS No. 68122-86-1] in isopropanol using a test article in which the dermal irritancy of undiluted Varisoft 475 would not be the limiting factor for the test. We believe that the NOEL which was reported in the Committee's summary document on quaternary ammonium compounds was calculated on the IQAC content basis.

Similarly, the PEQ study which is noted in the ITC letter was designed to allow for subchronic repeated dermal application of a test article which is irritant to the skin in undiluted form. The NOEL which was reported in the previously submitted summary document was, we believe, based on the PEQ content of the applied test article.

Figure 1: IQAC Compounds

CAS# 68122-86-1 Imidazolium compounds, 4,5-Dihydro-1-methyl-2-nortallow alkyl-1-(2-tallow amidoethyl), Methyl sulfates



CAS# 72623-82-6 Imidazolium compounds, 2-(C₁₃-C₁₇ alkyl)-1-[2-(C₁₄-C₁₈ amidoethyl)-4,5-dihydro-3-methyl], Methyl sulfates

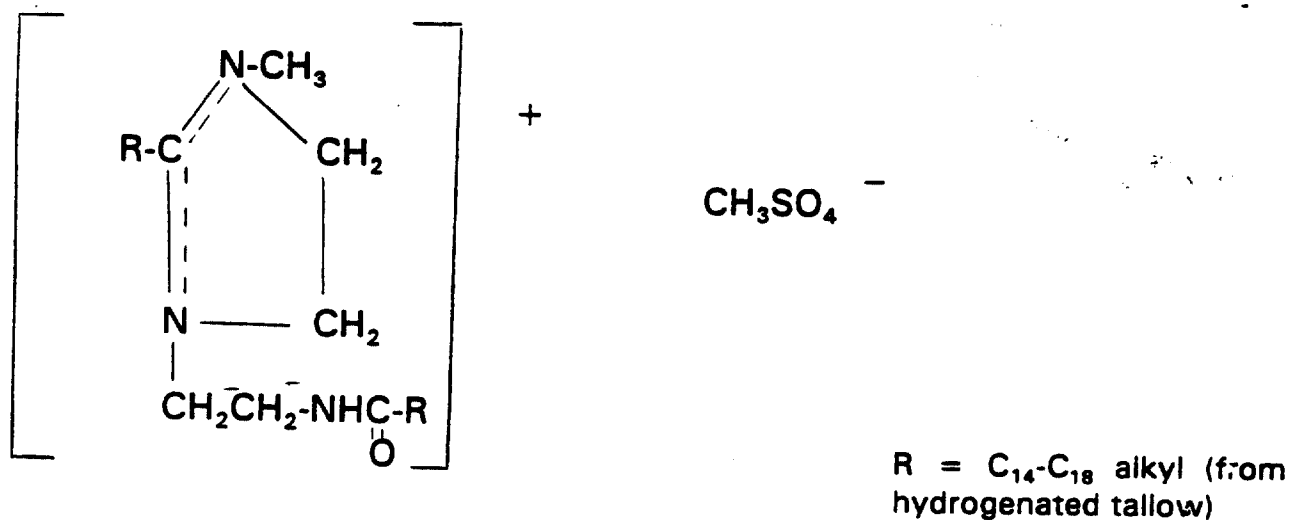


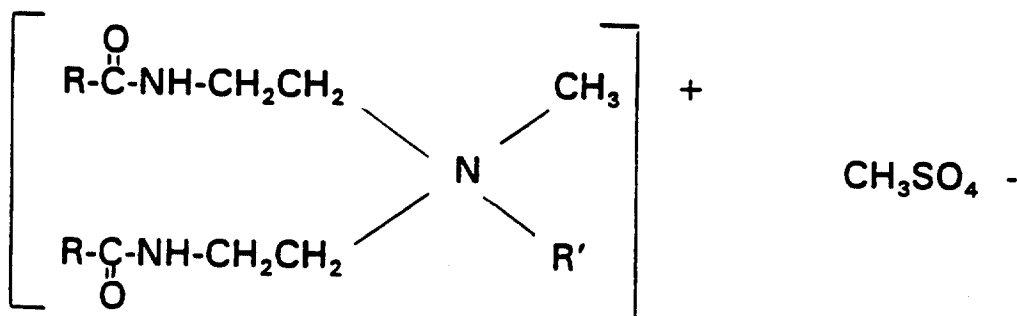
Figure 2: PEQ Compounds and EEQ Compounds

CAS# 68410-69-5 Poly (oxy-1,2-ethanediyl), α -[2-[bis (2-aminoethyl) methylammonio] ethyl]- ω -hydroxy-*N,N'*-ditallow acyl derivs., Me sulfate (salts)

CAS# 68389-89-9 Poly (oxy-1,2-ethanediyl), α -[2-[bis (2-aminoethyl) methylammonio] ethyl]- ω -hydroxy-*N,N'*-bis (hydrogenated tallow acyl) derivs., Me sulfate (salts)

CAS# 68413-04-7 Poly [oxy(methyl-1,2-ethanediyl)], α -[2-[bis (2-aminoethyl) methylammonio] methylethyl]- ω -hydroxy-*N,N'*-ditallow acyl derivs., Me sulfate (salts)

CAS# 68153-35-5 Ethanaminium, 2-amino-N-(2-aminoethyl)-*N*-(2-hydroxyethyl)-*N*-methyl, *N,N'*-ditallow acyl derivs., Me sulfate (salts)



For CAS# 68410-69-5:

R = tallow

R' = Poly (oxy-1,2-ethanediyl)

For CAS# 68389-89-9:

R = hydrogenated tallow

R' = Poly (oxy-1,2-ethanediyl)

For CAS# 68413-04-7:

R = tallow

R' = Poly [oxy (methyl-1,2-ethanediyl)]

For CAS# 68153-35-5:

R = tallow

R' = 2-hydroxyethyl



]

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 1:

**Report to Culver Chemical Company - Acute Oral
Toxicity Study on Culversoft S-75 in Albino Rats
[IQAC 68122-86-1]**

REPORT TO
CULVER CHEMICAL COMPANY
ACUTE ORAL TOXICITY STUDY ON
CULVERSOFT S-75
IN ALBINO RATS
IBT NO. A8214

I. Introduction

At the request of Culver Chemical Company an acute oral toxicity study was conducted on a yellow liquid identified as Culversoft S-75, 752.1 ml : 1 PA Lot No. 180636. The sample was shaken well immediately prior to use.

NOTE:

Please be advised that as of July 1, 1970, Northern Petrochemical Co. purchased Culver Chemical Co.

The name Culversoft S-75 was changed to Varisoft 475.

II. Summary -

An acute oral toxicity study was conducted on Culversoft S-75, Lot No. 180636. The test material was evaluated as is at dose levels of 10.2, 15.4, 23.1 and 34.6 g/kg. Four albino rats (two males and two females) were tested at each level. None of the animals dosed at the lower two levels died while three rats in the 23.1 g/kg group and all four animals in the 34.6 g/kg group died. The acute oral median lethal dose (LD₅₀) \pm the standard deviation was calculated to be 20.8 ± 2.1 g/kg. General signs of intoxication included the following: hypoactivity, ataxia, muscular weakness, diarrhea, prostration, and a ruffed fur. Necropsy of the animals that died revealed gastroenteritis. No gross pathologic alterations were noted among the animals sacrificed at the end of the observation period.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Carmen Mastri

Report prepared by: Carmen Mastri, B.S.
Section Head
Acute Toxicity Department

M. L. Keplinger

Report approved by: M. L. Keplinger, Ph.D.
Manager, Toxicology

Otis E. Fancher

Otis E. Fancher, Ph.D.
Director

III. Procedure

Healthy, young albino rats of the Charles River strain (COBS)* ranging in body weight from 150 to 200 grams were used as test animals. All animals used were kept under observation for five days prior to experimental use, during which period they were checked for general physical health and suitability as test animals. The animals were housed in stock cages and permitted a standard laboratory rat diet** plus water ad libitum until 16 hours immediately prior to oral intubation.

Initial screening was conducted in order to determine the general level of toxicity and then selected groups of four rats each (two male and two female) were intubated with previously calculated doses of the undiluted test material. All doses were administered directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-pointed intubating needle.

Following oral administration of the test material, the rats were housed individually in observation cages (10" x 8" x 8") and observed for the succeeding 14 days. Initial and final body weights as well as all mortalities and/or reactions displayed were recorded. Arrangements were made to autopsy any animal which might succumb during the study as well as all surviving animals at the end of the 14 days.

* Charles River Breeding Laboratories, Inc., North Wilmington, Massachusetts.

** Purina Rat Chow, Ralston Purina Company, St. Louis, Missouri.

At the end of the observation period, all data were collected and arrangements were made to calculate, if possible, the acute oral median lethal dose (LD₅₀) of the test material using the techniques of Weil*, Thompson**, and Thompson and Weil***.

* Weil, Carrol S.: Tables for Convenient Calculation of Median-Effective Dose (LD₅₀ or ED₅₀) and Instructions in Their Use. Biometrics, Sept. 1952.

** Thompson, William R.: Use of Moving Averages and Interpolation to Estimate Median-Effective Dose. Bact. Rev., Nov. 1947.

*** Thompson, William R. and Weil, Carrol S.: On the Construction of Tables for Moving Average Interpolation. Biometrics, March 1952.

IV. Results

A. Mortality and Body Weights

Individual mortality and body weight data are presented in Table I.

TABLE I

TEST MATERIAL: Culversoft S-75

Acute Oral Toxicity Study - Albino Rats

Mortality and Body Weight Data

Dose* (g/kg)	Animal Number and Sex	Individual Body Weights (grams)		<u>Number Dead</u> Number Tested	Percent Dead
		Test Day Number:			
		0	14		
10.2	1-M	206	308	0/4	0
	2-M	208	314		
	3-F	212	236		
	4-F	214	250		
15.4	5-M	204	298	0/4	0
	6-M	182	264		
	7-F	196	222		
	8-F	197	216		
23.1	9-M	171	255	3/4	75
	10-M	177	(2 days)		
	11-F	152	(2 days)		
	12-F	158	(5 days)		
34.6	13-M	180	(2 days)	4/4	100
	14-M	165	(3 days)		
	15-F	170	(2 days)		
	16-F	152	(4 days)		

Note: Figures in parentheses indicate time of death.

Acute Oral LD₅₀ = 20.8 g/kg

Standard Deviation of LD₅₀ = ± 2.1 g/kg

* Culversoft S-75 was administered as is.

B. Reactions

The reactions exhibited by the animals following oral administration of Culversoft S-75 are presented in Table II.

Necropsy of the animals that died revealed gastroenteritis. No gross pathologic alterations were noted among any of the animals sacrificed at the end of the 14-day observation period.

TABLE II

TEST MATERIAL: Culversoft S-75

Acute Oral Toxicity Study - Albino Rats

Summary of Reactions

Dose (g/kg)	Reaction	Time of Onset Following Dose Administration (hours)	Duration of Reaction (days)	Time of Death Following Dose Administration (days)
10.2	Hypoactivity Ruffed fur	1/2	2	-
		6-22	1	-
15.4	Hypoactivity Ruffed fur Muscular weakness Diarrhea	1/2	3	-
		6-22	2	-
		6-22	2	-
		6-22	2	-
23.1	Hypoactivity Ataxia Muscular weakness Prostration Diarrhea Ruffed fur	1/2	5	2-5
		1	6-22 hours	
		1	2	
		5	2	
		6-22	2	
		6-22	4	
34.6	Hypoactivity Ataxia Muscular weakness Prostration Diarrhea Ruffed fur	1/2	Until death	2-4
		1/2		
		1		
		1		
		6-22		
		6-22		



]

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 2:

**Toxicity Studies for Ashland Oil Company
[IQAC 68122-86-1, misc. formulations]**

TOXICITY STUDIES
FOR
ASHLAND OIL COMPANY

COMPILED BY:
M. Patricia Prate

REPORTED:
December 18, 1973

REQUESTED BY:
Dr. N.S. Salomons

Bio-Toxicology Laboratories, Inc.

Twin Oak Farm Division
Creek & Cox Roads, P. O. Box 267, Moorestown, N. J. 08057
Phone: (609) 665-1776 — 235-2908

December 18, 1973

Dr. N.S. Salomons
Ashland Oil, Inc.
5200 Blazer Parkway
Dublin, Ohio 43017

Dear Dr. Salomons:

Following are the results of the experimental procedures conducted for Ashland Oil, Inc.

MATERIAL:

Varisoft 475
Varisoft 475
(5% free amine)
Varisoft 475
(13.5 wt. % solids)
Varisoft 475
(13.5 wt. % solids -
5% free amine)

RECEIVED:

November 21, 1973

EXPERIMENTAL PERIOD:

November 26 - December 18, 1973

EXPERIMENTAL PROCEDURES:

Eye Irritation Study
Primary Irritation Study
Acute Oral LD50 Study

The conclusions in this study are based upon the results of the study completed December 18, 1973.

This report is submitted for the exclusive use of Ashland Oil, Inc.

JDP/lsd



Very truly yours,

John Davis Paul
John Davis Paul
President

EYE IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 475 (13.5 wt.% solids)

Varisoft 475 (13.5 wt.% solids -5% free amine)

DRAIZE RABBIT EYE IRRITATION STUDY PROCEDURE

FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

A group of 12 albino rabbits was used in this study to determine the toxicity of the substances submitted to eye mucosa. A series of 6 rabbits was used for testing each substance.

One tenth of a milliliter of the product under test was instilled into the conjunctival sacs of the test animals. All treated eyes were unwashed. Ocular evaluations were made with the unaided eye. These evaluations were made at 24, 48 and 72 hours.

The cornea is scored on the basis of the density of the opacity and the total area involved. The iris is scored on the intensity or degree of inflammation exhibited; and the palpebral and bulbar mucosae are scored on the extent of chemosis, hyperemia and discharge.

DRAIZE SCALE FOR SCORING OCULAR LESIONS

1. Cornea
 - A. Opacity-Degree of Density (area which is most dense taken for reading)

Scattered or diffuse area-details of iris clearly visible.....	1
Easily discernible translucent areas, details of iris slightly obscured.....	2
Opalescent areas, no details of iris visible, size of pupil barely discernible.....	3
Opaque, iris invisible.....	4
 - B. Area of Corneal damage involved

One quarter of area (or less) but not zero.....	1
Greater than one quarter, less than one-half.....	2
Greater than one half, less than three quarters.....	3
Greater than three quarters up to whole area.....	4

Score equals A x B x 5 Total maximum - 80

2. Iris
 - A. Values

Folds above normal, congestion, swelling circumcorneal injection (any one or all of these or combination of any thereof), iris still reacting to light, (sluggish reaction is positive).....	1
No reaction to light, hemorrhage; gross destruction (any one or all of these).....	2

Score equals A x 5 Total possible maximum - 10

3. Conjunctivae
 - A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Vessels definitely injected above normal.....	1
More diffuse, deeper crimson red, individual vessels not easily discernible.....	2
Diffuse beefy red.....	3
 - B. Chemosis

Any swelling above normal (includes nictitating membrane).....	1
Obvious swelling with partial eversion of the lids.....	2
Swelling with lids about half closed.....	3
Swelling with lids about half closed to completely closed.....	4
 - C. Discharge

Any amount different from normal (does not include small amount observed in inner canthus of normal animals).....	1
Discharge with moistening of the lids and hairs just adjacent to the lids.....	2
Discharge with moistening of the lids and considerable area around eye.....	3

Score (A + B + C) x 2 Total maximum - 20

The maximum total score is the sum of all scores obtained for the cornea, iris and conjunctivae. Total maximum score possible - 110 points

BASIS OF CLASSIFICATION AND CONCLUSIONS

The following arbitrary designation of classification is offered as a guide in judging the severity of a compound when subjected to the Draize Eye Irritation Technique. This classification is subject to immediate revision upon suggestion or directive, from municipal or federal governmental agencies.

Conclusions in this report are based upon the particular samples and animals employed, temperature variants, and other conditions controllable or uncontrollable by the physicians, veterinarians, technicians, operators, observers and compilers of this study and report.

CLASSIFICATION KEY

O = duration and magnitude of irritation, comparable to distilled water

I = mild irritant (total points scored/day less than 10; no score under cornea or iris)

II = moderate irritant (total points scored/day less than 15; no score under cornea or iris)

III = strong irritant (total points scored/day 15 or more; no score under cornea or iris)

SUB-GROUPINGS

A = short duration (zero score on or before third day)

B = moderate duration (zero score by fourth or fifth day)

C = long duration (zero score by sixth or seventh day)

D = prolonged duration (score on seventh day)

E = temporary corneal or iris lesions (not apparent on seventh day)

F = permanent corneal or iris lesions (continuing past seventh day)

Example: III A to III DF --- indicates compound is a strong irritant of short to prolonged duration, capable of producing permanent corneal or iris lesions, when instilled into the eyes of albino rabbits.

SCORE SHEET

Varisoft 475 (13.5 wt. % solids)

Varisoft 475 (13.5 wt. % solids - 5% free amine)

Animal No. 1 Unwashed

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt.% solids)

Animal No. 2 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1	1	
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2	2	

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
(13.5 wt.% solids)

Animal No. 3 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1		
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2		

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt. % solids)

Animal No. 4 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1	1	
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2	2	

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested **Varisoft 475**
 (13.5 wt. % Solids)

Animal No. **5 Unwashed**

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1		
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2		

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0
Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt. % Solids)

Animal No. 6 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1		
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2		

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt. % solids -
 5% free amine)

Animal No. 1 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1		
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2		

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

d Varisoft 475
 (13.5 wt.% solids -
 5% free amine)

2 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1		
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2		

ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

for ton: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt. % solids -
 5% free amine)

Animal No. 3 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1	1	
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2	2	

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

DRAIZE RABBIT EYE IRRITATION STUDY
Federal Hazardous Substances Labeling Act

Product Tested Varisoft 475
 (13.5 wt. % solids -
 5% free amine)

Animal No. 4 Unwashed

Hours	24	48	72
I- CORNEA			
A- Opacity			
B- Area Involved			
II- IRIS			
A- Evaluation			
III- CONJUNCTIVAE			
A- Hyperemia	1	1	
B- Chemosis			
C- Discharge			
Total Points (Total Possible 110)	2	2	

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

Classification: I.A.

SUMMARY OF POINTS SCORED

Varisoft 475 (13.5 wt. % solids)
Varisoft 475 (13.5 wt.% solids - 5% free amine)

SUMMARY OF POINTS SCORED

[illegible]

PRIMARY IRRITATION STUDY

Department of Transportation Act

Varisoft 475

Varisoft 475 (5% Free Amine)

Varisoft 475 (13.5 wt. % Solids)

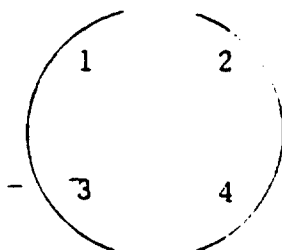
Varisoft 475 (13.5 wt. % Solids - 5% Free Amine)

METHOD FOR PRIMARY IRRITATION
DEPARTMENT OF TRANSPORTATION ACT

The intact and abraded skin of 24 albino rabbits was employed for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Four areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. Areas 2 and 3 were abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch). The patches consisted of 1.5 inch x 1.5 inch 12 ply gauze squares. The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml. for liquids and 0.5 gm. for solids) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retard evaporation of volatile substances during the four hour exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis of weighted scores.

Following this initial reading, all test sites were washed with appropriate solvent to prevent further exposure. Readings were again made at 24 and 48 hours after the initial application. Each test substance is evaluated on a total of six sites (6 abraded and 6 intact).

The primary irritation index is calculated by adding the values for erythema or eschar formation, and edema at 4, 24 and 48 hours on intact and abraded skin (12 values) and dividing by six to obtain an individual score on each rabbit.



2 and 3 = abraded

1 and 4 = intact

1 and 2 = control (if employed)

3 and 4 = test material

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

A. Erythema and Eschar Formation	
Very slight erythema (barely perceptible).....	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4
<hr/>	
Total possible erythema score.....	4
<hr/>	
B. Edema Formation	
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm.).....	3
Severe edema (raised more than 1 mm. and extending beyond area of exposure).....	4
<hr/>	
Total possible edema score.....	4
<hr/>	
Total possible score for primary irritation.....	8
or sensitization.....	8
<hr/>	

Primary Irritation Index

2 or less.....mild irritant
2 - 5.....moderate irritant
6 or above.....severe irritant

Sensitization

2 or less.....mild sensitizer
2 - 5.....moderate sensitizer
6 or above.....severe sensitizer

SCORE SHEETS

Varisoft 475

Varisoft 475 (5% free amine)

Varisoft 475 (13.5 wt.% solids)

Varisoft 475 (13.5 wt. % solids - 5% free amine)

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 475

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	1	1	0	0	0	0	0.83
	Abraded	2	1	0	0	0	0	
2	Intact	1	0	0	0	0	0	0.50
	Abraded	1	1	0	0	0	0	
3	Intact	1	1	0	0	0	0	0.66
	Abraded	1	1	0	0	0	0	
4	Intact	1	0	0	0	0	0	0.83
	Abraded	2	1	1	0	0	0	
5	Intact	1	1	0	0	0	0	0.83
	Abraded	2	1	0	0	0	0	
6	Intact	1	1	0	0	0	0	1.16
	Abraded	2	2	1	0	0	0	

PRIMARY IRRITATION INDEX OF COMPOUND 0.8 (mild primary irritant)

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 475
(5% Free Amine)

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	1	1	1	0	0	0	1.83
	Abraded	2	2	1	0	1	1	
2	Intact	1	1	0	0	0	0	2.00
	Abraded	3	2	2	0	2	1	
3	Intact	1	0	0	0	0	0	1.00
	Abraded	2	1	1	0	1	0	
4	Intact	1	1	0	0	0	0	1.83
	Abraded	2	2	2	0	2	1	
5	Intact	1	1	1	0	0	0	1.66
	Abraded	3	2	1	0	1	0	
6	Intact	1	0	0	0	0	1	1.66
	Abraded	2	2	1	0	2	1	

PRIMARY IRRITATION INDEX OF COMPOUND 1.7 (mild primary irritant)

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 475
(13.5 wt. % solids)

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	1	1	0	0	0	0	0.66
	Abraded	1	1	0	0	0	0	
2	Intact	1	0	0	0	0	0	0.50
	Abraded	1	1	0	0	0	0	
3	Intact	0	0	0	0	0	0	0.50
	Abraded	1	1	1	0	0	0	
4	Intact	1	1	1	0	0	0	1.00
	Abraded	1	1	1	0	0	0	
5	Intact	0	0	0	0	0	0	0.33
	Abraded	1	1	0	0	0	0	
6	Intact	1	0	0	0	0	0	0.66
	Abraded	1	1	1	0	0	0	

PRIMARY IRRITATION INDEX OF COMPOUND 0.6 (mild primary irritant)

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 475
 (13.5 wt. % solids
 5% Free Amine)

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	1	1	0	0	0	0	1.33
	Abraded	2	1	1	0	1	1	
2	Intact	1	1	0	0	0	0	1.50
	Abraded	2	2	1	0	1	1	
3	Intact	1	1	0	0	0	0	1.66
	Abraded	2	2	1	0	2	1	
4	Intact	1	1	0	0	0	0	1.50
	Abraded	2	2	1	0	1	1	
5	Intact	1	0	0	0	0	0	0.83
	Abraded	1	1	1	0	1	0	
6	Intact	1	1	0	0	0	0	1.17
	Abraded	2	1	1	0	1	0	

PRIMARY IRRITATION INDEX OF COMPOUND 1.3 (mild primary irritant)

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 475

Varisoft 475 (5% Free Amine)

Varisoft 475 (13.5 wt. % Solids)

Varisoft 475 (13.5 wt. % Solids - 5% Free Amine)

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN
FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of 24 albino rabbits was used for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

A. Erythema and Eschar Formation	
Very slight erythema (barely perceptible).....	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4
<hr/>	
Total possible erythema score.....	4
<hr/>	
B. Edema Formation	
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm.).....	3
Severe edema (raised more than 1 mm. and extending beyond area of exposure).....	4
<hr/>	
Total possible edema score.....	4
<hr/>	
Total possible score for primary irritation.....	8
or sensitization.....	8
<hr/>	

Primary Irritation Index

2 or less.....mild irritant
 2 - 5.....moderate irritant
 6 or above.....severe irritant

Sensitization

2 or less.....mild sensitizer
 2 - 5.....moderate sensitizer
 6 or above.....severe sensitizer

SCORE SHEETS

Varisoft 475

Varisoft 475 (5% free amine)

Varisoft 475 (13.5 wt. % solids)

Varisoft 475 (13.5 wt. % solids-
5% free amine)

PRIMARY IRRITATION STUDY

risoft 475

ize Woodard and Calvery

RABBIT SKIN				COMBINED AVERAGE
INTACT		ABRADED		
	72 HRS.	24 HRS.	72 HRS.	
	0/0	1/0	0/0	0.92
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	2/0	0/0	
0.67			1.17	

of Compound 0.92

PRIMARY IRRITATION STUDY

Product Tested

Varisoft 475
(5% Free Amine)

Test Method

Draize Woodard and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBINED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
1	M	1/0	0/0	2/1	1/0	2.55
2	F	1/0	0/0	2/2	1/0	
3	F	0/0	0/0	1/1	0/0	
4	M	0/0	0/0	2/2	1/0	
5	M	1/0	0/0	1/1	0/0	
6	F	0/0	0/0	2/2	1/0	
AVERAGE		0.67		3.83		

Primary Irritation Index of Compound 2.55

Erythema/Edema

PRIMARY IRRITATION STUDY

soft 475

5% wt. solids)

Woodard and Calvery

RABBIT SKIN				COMBINED AVERAGE
CONTACT		ABRADED		
	72 HRS.	24 HRS.	72 HRS.	
	0/0	1/0	0/0	0.75
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	1/0	0/0	
	0/0	1/0	0/0	
0.5			1.0	

Compound 0.75

PRIMARY IRRITATION STUDY

Product Tested

Varisoft 475
(13.5 wt. % solids - 5% free amine)

Test Method

Draize Woodard and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBINED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
1	M	1/0	0/0	1/1	0/0	1.92
2	F	1/0	0/0	2/1	1/0	
3	F	1/0	0/0	2/2	0/0	
4	M	1/0	0/0	2/1	0/0	
5	M	0/0	0/0	1/1	0/0	
6	F	1/0	1/0	1/1	0/0	
AVERAGE		1.0		2.83		

Primary Irritation Index of Compound 1.92

Erythema/Edema

ACUTE ORAL LD50 TOXICITY STUDY

Varisoft 475 (13.5 wt. % solids)

Varisoft 475 (13.5 wt. % solids - 5% free amine)

METHOD - ACUTE ORAL TOXICITY

A group of approximately 30 albino male and female rats, fasted for twenty-four hours were employed to establish an LD₅₀ range for each product under test.

Young adult rats which had not been used for previous test purposes were assigned to various dose levels at random. Both sexes were equally distributed.

The product under test was placed in a glass syringe and introduced through the esophagus into the stomach with a stainless steel catheter.

Animals on the same dosage level were then placed in a common cage with free access to food and water. The animals were observed daily for a two week period. No postmortem, or histopathology examinations were performed in this particular study.

SCORE SHEETS

Varisoft 475 (13.5 wt.% solids)
Varisoft 475 (13.5 wt.% solids - 5% Free Amine)

ACUTE ORAL TOXICITY ASSAY

Varisoft 475
(13.5 wt. % Solids)
EXPERIMENTAL DATA

Dosages 0.5 cc./Kg. - 16.0 cc./Kg.

Animals Fasted male & female albino rats

Concentration Undiluted (as received)

Weights 200-300 grams

Group No.	No. Animals	Dose Level	Number and Day of Deaths														Total	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	S*	D*
I	5	0.5 cc./Kg.															5	0
II	5	1.0 cc./Kg.															5	0
III	5	2.0 cc./Kg.															5	0
IV	5	4.0 cc./Kg.															5	0
V	5	8.0 cc./Kg.															5	0
VI	5	16.0 cc./Kg.															5	0
VII		cc./Kg.																
VIII		cc./Kg.																
IX		cc./Kg.																
X		cc./Kg.																

OBSERVATIONS:

Animals dosed at 0.5 cc./Kg. - 2.0 cc./Kg. did not exhibit any effects from the test material.

At the 4.0 cc./Kg. and 8.0 cc./Kg. dosage levels, slightly unkempt coats were noted for approximately 24 hours after forced feeding.

The animals dosed at 16.0 cc./Kg. exhibited slightly unkempt coats after dosing. Normalcy returned within 2-3 days.

Equally non-toxic to males & females.

LD₀ = Over 16.0 cc./Kg.

LD₅₀ = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

LD₁₀₀ = Over 16.0 cc./Kg.

* D = Deaths

* S = Survivals

ACUTE ORAL TOXICITY ASSAY

Varisoft 475 (13.5 wt. %
solids - 5% free amine)
EXPERIMENTAL DATA

Dosages 0.5 cc./Kg. - 16.0 cc./Kg.

Animals Fasted male & female albino rats

Concentration Undiluted (as received)

Weights 200-300 grams

Group No.	No. Animals	Dose Level	Number and Day of Deaths														Total	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	S*	D*
I	5	0.5 cc./Kg.															5	0
II	5	1.0 cc./Kg.															5	0
III	5	2.0 cc./Kg.															5	0
IV	5	4.0 cc./Kg.															5	0
V	5	8.0 cc./Kg.															5	0
VI	5	16.0 cc./Kg.															5	0
VII		cc./Kg.																
VIII		cc./Kg.																
IX		cc./Kg.																
X		cc./Kg.																

OBSERVATIONS:

Animals dosed at 0.5 cc./Kg. - 2.0 cc./Kg. did not exhibit any effects from the test material.

At the 4.0 cc./Kg. and 8.0 cc./Kg. dosage levels, slightly unkempt coats were noted for approximately 24 hours after forced feeding.

The animals dosed at 16.0 cc./Kg. exhibited slightly unkempt coats after dosing. Normalcy returned within 2-3 days.

Equally non-toxic to males & females.

LD₀ = Over 16.0 cc./Kg.

LD₅₀ = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

LD₁₀₀ = Over 16.0 cc./Kg.

* D = Deaths

* S = Survivals

SUMMARY & CONCLUSIONS

Varisoft 475

Varisoft 475 (5% free amine)

Varisoft 475 (13.5 wt. % solids)

Varisoft 475 (13.5 wt. % solids - 5% free amine)

RESULTS & CONCLUSIONS

QUALITY DATA

Varisoft 475

Individual Score Sheets

Detailed Information)

STUDIES PERFORMED

DRAIZE EYE IRRITATION

X PRIMARY IRRITATION

ACUTE ORAL TOXICITY

DRAIZE EYE IRRITATION STUDY						
albino rabbits						
TREATMENT	eyes unwashed		eyes washed		eyes washed	
	Total Points	Mean Value	Total Points	Mean Value	Total Points	Mean Value
Control						
Test						
Reactive						
Requires labeling under the Federal Hazardous Substances Act.						
Does not require labeling under the Federal Hazardous Substances Act.						

1. IRRITATION STUDY - F.H.S.L.A. Procedure	6 albino rabbits
Primary Irritation Index:	0.92 (mild primary irritant)

PRIMARY IRRITATION STUDY - D.O.T. Procedure				
6 albino rabbits				
Primary Irritation Index: 0.8 (mild primary irritant)				
Site	Evaluation of Skin Reaction	Ratio regarding six rabbits		
		Observation time		
		4 hrs.	24 hrs.	48 hrs.
Test	Non-Corrosive	6:6	6:6	6:6
Control	Non-Corrosive	6:6	6:6	6:6

ACUTE ORAL TOXICITY		Acute Oral LD ₅₀ Study - 30 albino rats
(single parenteral dose)		F.H.S.L.A. Procedure - 10 albino rats
Acute Oral LD ₅₀ Study:		Federal Hazardous Substances Act Procedure:
LD ₅₀	95% Confidence Limits	Dosage: 5.0 c.c. or 5.0 gms./Kg.
		Deaths:
Requires labeling under the Federal Hazardous Substances Act.		
Does not require labeling under the Federal Hazardous Substances Act.		

**SUMMARY & CONCLUSIONS
OF TOXICITY DATA**

SAMPLE Varisoft 475

(5% Free Amine)

(See Individual Score Sheets
for Detailed Information)

STUDIES PERFORMED

DRAIZE EYE IRRITATION

X PRIMARY IRRITATION

ACUTE ORAL TOXICITY

DRAIZE EYE IRRITATION STUDY						
STRUCTURE	eyes unwashed		eyes washed		eyes washed	
	Total	Mean	Total	Mean	Total	Mean
	Points	Value	Points	Value	Points	Value
Cornea						
Iris						
Conjunctivae						
Requires labeling under the Federal Hazardous Substances Act. Does not require labeling under the Federal Hazardous Substances Act.						

PRIMARY IRRITATION STUDY - F.H.S.L.A. Procedure	6 albino rabbits
Primary Irritation Index: 2.25 (moderate primary irritant)	

PRIMARY IRRITATION STUDY - D.O.T. Procedure			6 albino rabbits	
Primary Irritation Index: 1.7 (mild primary irritant)				
		Ratio regarding six rabbits		
	Evaluation of	Observation time		
Test Site	Skin Reaction	4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

ACUTE ORAL TOXICITY (single parenteral dose)	Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats
Acute Oral LD ₅₀ Study:	Federal Hazardous Substances Act Procedure:
LD ₅₀ - 95% Confidence Limits	Dosage: 5.0 c.c. or 5.0 gms./Kg. Deaths:
Requires labeling under the Federal Hazardous Substances Act. Does not require labeling under the Federal Hazardous Substances Act.	

**SUMMARY & CONCLUSIONS
OF TOXICITY DATA**

SAMPLE Varisoft 475
(13.5 wt. % solids)
(See Individual Score Sheets
for Detailed Information)

STUDIES PERFORMED

X DRAIZE EYE IRRITATION
X PRIMARY IRRITATION
X ACUTE ORAL TOXICITY

DRAIZE EYE IRRITATION STUDY			6 albino rabbits			
STRUCTURE	6 eyes unwashed		eyes washed		eyes washed	
	Total Points	Mean Value	Total Points	Mean Value	Total Points	Mean Value
Cornea	0	0.0				
Iris	0	0.0				
Conjunctivae	16	2.7				
Requires labeling under the Federal Hazardous Substances Act.						
X Does not require labeling under the Federal Hazardous Substances Act.						

PRIMARY IRRITATION STUDY - F.H.S.L.A. Procedure			6 albino rabbits
Primary Irritation Index:		0.75 (mild primary irritant)	

PRIMARY IRRITATION STUDY - D.O.T. Procedure			6 albino rabbits	
Primary Irritation Index: 0.6 (mild primary irritant)				
		Ratio regarding six rabbits		
	Evaluation of	Observation time		
Test Site	Skin Reaction	4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

ACUTE ORAL TOXICITY (single parenteral dose)		X Acute Oral LD ₅₀ Study - 30 albino rats
Acute Oral LD ₅₀ Study:		F.H.S.L.A. Procedure - 10 albino rats
LD ₅₀ - 95% Confidence Limits		Federal Hazardous Substances Act Procedure:
Over 16.0 cc./Kg.		Dosage: 5.0 c.c. or 5.0 gms./Kg.
Not Established		Deaths:
Requires labeling under the Federal Hazardous Substances Act.		
X Does not require labeling under the Federal Hazardous Substances Act.		

SUMMARY & CONCLUSIONS

OF TOXICITY DATA

SAMPLE Varisoft 475

(13.5 wt. % solids - 5% free amine)

(See Individual Score Sheets
for Detailed Information)

STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- X ACUTE ORAL TOXICITY

DRAIZE EYE IRRITATION STUDY						
6 albino rabbits						
STRUCTURE	6 eyes unwashed		eyes washed		eyes washed	
	Total Points	Mean Value	Total Points	Mean Value	Total Points	Mean Value
Cornea	0	0.0				
Iris	0	0.0				
Conjunctivae	18	3.0				
Requires labeling under the Federal Hazardous Substances Act.						
X Does not require labeling under the Federal Hazardous Substances Act.						

PRIMARY IRRITATION STUDY - F.H.S.L.A. Procedure		6 albino rabbits
Primary Irritation Index:		1.92 (mild primary irritant)

PRIMARY IRRITATION STUDY - D.O.T. Procedure				6 albino rabbits
Primary Irritation Index:		1.3 (mild primary irritant)		
Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits		
		Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

ACUTE ORAL TOXICITY		X	Acute Oral LD ₅₀ Study - 30 albino rats
(single parenteral dose)			F.H.S.L.A. Procedure - 10 albino rats
Acute Oral LD ₅₀ Study:			Federal Hazardous Substances Act Procedure:
LD ₅₀ - 95% Confidence Limits			Dosage: 5.0 c.c. or 5.0 gms./Kg.
Over 16.0 cc./Kg. Not Established			Deaths:
Requires labeling under the Federal Hazardous Substances Act.			
X Does not require labeling under the Federal Hazardous Substances Act.			

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 3:

Report to Northern Petrochemical Company -
Eye Irritation Tests with Eleven Samples in Albino Rabbits
[IQAC 68122-86-1, 5% dispersion]

REPORT TO
NORTHERN PETROCHEMICAL COMPANY
EYE IRRITATION TESTS WITH
ELEVEN SAMPLES
IN ALBINO RABBITS

IBT NO. A2182

I. Introduction

At the request of Northern Petrochemical Company, an eye irritation test was conducted with each of eleven samples. The samples were identified as follows:

1. Varsulf 142-37, Lot 156-23, 20% Dispersion
2. Varsulf 142-37A, 20% Dispersion
3. Varifos 156-27, 20% Dispersion
4. Varisoft E228, Lot V12-201222, 5% Dispersion
5. Varisoft 475, Lot V34-207309, 5% Dispersion
6. Varisoft 3690, Lot V9-209123, 5% Dispersion
7. Varisoft SDC, Lot V12-110320, 5% Dispersion
8. Varisoft 3262, Ref. 157-8B, 5% Dispersion
9. Varisoft 100, Ref. 157-8A, 5% Dispersion
10. Adogen 432, Ref. 157-8C, 5% Dispersion
11. Varisoft 136-62, 5% Dispersion

II. Summary


The results of the rabbit eye irritation tests conducted with eleven samples are summarized below.

<u>Test Material</u>	<u>% Dispersion</u>	<u>Results</u>	
		<u>Maximum Mean Irritation Score</u>	<u>Rating</u>
Varsulf 142-37	20	21.7/110.0	Mildly Irritating
Varsulf 142-37A	20	18.3/110.0	Mildly Irritating
Varifos 156-27	20	41.3/110.0	Moderately Irritating
Varisoft E228	5	62.0/110.0	Extremely Irritating
Varisoft 475	5	11.3/110.0	Minimally Irritating
Varisoft 3690	5	12.0/110.0	Mildly Irritating
Varisoft SDC	5	86.3/110.0	Extremely Irritating
Varisoft 3262	5	12.6/110.0	Minimally Irritating
Varisoft 100	5	15.7/110.0	Mildly Irritating
Adogen 432	5	84.0/110.0	Extremely Irritating
Varisoft 136-62	5	17.0/110.0	Mildly Irritating

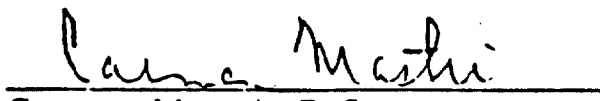
Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:


Kenneth Ebbens, B.S.
Assistant Toxicologist
Acute Toxicity

Report approved by:


Carmen Mastri, B.S.
Senior Group Leader
Acute Toxicity


M. L. Keplinger, Ph.D.
Manager, Toxicology

III. Investigational Procedure

The same procedure was followed for each test material.

Young albino rabbits of the New Zealand strain were used to evaluate the eye irritating properties of the test material. The test method was patterned after that of Draize et al.*

The test material was instilled into the conjunctival sac of the right eye of each rabbit according to the treatment procedure presented in Table I. The left eye of each animal served as a control. At each scoring interval the cornea, iris, and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system*. The maximum possible score at any one examination and scoring period is 110 points, which indicates maximal irritation and damage to all three ocular tissues. Zero score indicates no irritation. The scoring system is presented in Table II. In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After the completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test material. The criteria used for assignment of the descriptive rating are the frequency, the extent, and the persistence of irritation or damage which occur to the three ocular tissues.

* Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

TABLE I
Eye Irritation Tests - Albino Rabbits

Treatment Procedure						
Test Material	Number of Animals Evaluated	Form Administered	Quantity of Test Material Administered	Contact Period (seconds)	Volume of Wash (tap water)	Scoring Intervals
Varsulf 142-37, 20%	3	Undiluted	0.1 ml	Unlimited	None	One minute, one, 24 and 72 hours, and 7 days
Varsulf 142-37A, 20%	3	Undiluted	0.1 ml	Unlimited	None	One minute, one, and 72 hours, and 7 days
Varifos 156-27, 20%	3	Undiluted	0.1 ml	Unlimited	None	One minute, one, 24 and 72 hours, and 7 and 14 days
Varisoft E228, 5%	3	Undiluted	0.1 ml	Unlimited	None	One, 24 and 72 hours, and 7 and 14 days
Varisoft 475, 5%	3	Undiluted	0.1 ml	Unlimited	None	One minute, one, 24 and 72 hours, and 7 days
Varisoft 3690, 5%	3	Undiluted	0.1 ml	Unlimited	None	One minute, one, 24 and 72 hours, and 7 days
Varisoft SDC, 5%	3	Undiluted	0.1 ml	Unlimited	None	One, 24 and 72 hours, and 7 and 14 days
Varisoft 3262, 5%	3	Undiluted	0.1 ml	Unlimited	None	One, 24 and 72 hours, and 7 days

TABLE I (continued)

Eye Irritation Tests - Albino Rabbits

Treatment Procedure

Test Material	Number of Animals Evaluated	Treatment Procedure			Scoring Intervals
		Form Administered	Quantity of Test Material Administered	Contact Period (seconds)	
Varisoft 100, 5%	3	Undiluted	0.1 ml	Unlimited	One minute, one, 24 and 72 hours, and 7 days
Adogen 432, 5%	3	Undiluted	0.1 ml	Unlimited	One minute, one, 24 and 72 hours, and 7 and 14 days
Varisoft 136-62, 5%	3	Undiluted	0.1 ml	Unlimited	One, 24 and 72 hours, and 7 days

TABLE II

Eye Irritation Tests - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description.	Grading
Cornea	<u>Opacity (A)</u>	
	Opacity - Degree of density (area which is dense is taken for reading).	
	Scattered or diffuse area, details of iris clearly visible.	1
	Easily discernible translucent areas, details of iris slightly obscured.	2
	Opalescent areas, no details of iris visible, size of pupil barely discernible.	3
	Opaque, iris invisible.	4
	<u>Area of Cornea Involved (B)</u>	
	One quarter (or less) but not zero.	1
	Greater than one-quarter but less than one-half,	2
	Greater than one-half but less than three-quarters.	3
	Greater than three-quarters, up to whole area.	4
	Score equals $A \times B \times 5$	Total maximum = 80
Iris	<u>Values (A)</u>	
	Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive).	1
	No reaction to light, hemorrhage, gross destruction (any or all of these).	2
	Score equals $A \times 5$	Total maximum = 10

TABLE II continued

Eye Irritation Tests - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Grading
Conjunctiva	<u>Redness (A)</u>	
	Redness (refers to palpebral conjunctiva only). Vessels definitely injected above normal.	1
	More diffuse, deeper crimson red, individual vessels not easily discernible.	2
	Diffuse beefy red.	3
	<u>Chemosis (B)</u>	
	Any swelling above normal (includes nictitating membrane).	1
	Obvious swelling with partial eversion of the lids.	2
	Swelling with lids about half-closed.	3
	Swelling with lids about half-closed to completely closed.	4
	<u>Discharge (C)</u>	
	Any amount different from normal (does not in- clude small amount observed in inner canthus of normal animals).	1
	Discharge with moistening of the lids and hairs just adjacent to the lids.	2
	Discharge with moistening of the lids and hairs and considerable area around eye.	3
Score (A + B + C) x 2		Total maximum = 20

Note: The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctiva.

The rating is arrived at by selecting the maximum mean irritation score at one, 24 or 72 hours after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table III.

TABLE III

Eye Irritation Tests - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Non-Irritating	0.0 - 0.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level.
Practically Non-Irritating	> 0.5 - 2.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level.
Minimally Irritating	> 2.5 - 15.0	To maintain this rating, all scores at the 72-hour reading must be zero; otherwise, increase rating one level.
Mildly Irritating	>15.0 - 25.0	To maintain this rating, all scores at the 7-day reading must be zero; otherwise, increase rating one level.
Moderately Irritating	>25.0 - 50.0	To maintain this rating, scores at 7 days must be ≤ 10 for 60% or more of the animals. Also, mean 7-day score must be ≤ 20 . If 7-day mean score is ≤ 20 but $< 60\%$ of animals show scores < 10 , then no animal among those showing scores > 10 can exceed a score of 30 if rating is to be maintained; otherwise, raise rating one level.

TABLE III continued

Eye Irritation Tests - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Severely Irritating	>50.0 - 80.0	To maintain this rating, scores at 7 days must be ≤ 30 for 60% or more of the animals. Also, mean 7-day score must be ≤ 40 . If 7-day mean score is ≤ 40 but <60% of the animals show scores ≤ 30 , then no animal among those showing scores > 30 can exceed a score of 60 if rating is to be maintained; otherwise, raise rating one level.
Extremely Irritating	>80.0 - 110.0	

IV. Results

The results of the eye irritation tests are presented in Tables

IV - XIV

TABLE VIII

TEST MATERIAL: Varisoft 475

Eye Irritation Test - Albino Rabbits

Cults

Issue	Rabbit Number	1			24			72			7		
		Minute	Hour		Hours			Hours			Days		
Cornea (D-A) Iris Conjunctiva (R-S-D) Total	1	0	0		5 (1-1)			0			0		
		0	0		0			0			0		
		8 (2-1-1)	12 (2-2-2)		4 (1-1-0)			0			0		
		8	12		9			0			0		
Cornea (D-A) Iris Conjunctiva (R-S-D) Total	2	0	0		0			0			0		
		0	0		0			0			0		
		6 (2-0-1)	12 (2-2-2)		4 (1-1-0)			0			0		
		6	12		4			0			0		
Cornea (D-A) Iris Conjunctiva (R-S-D) Total	3	0	0		0			0			0		
		0	0		0			0			0		
		6 (2-0-1)	10 (2-1-2)		4 (1-1-0)			0			0		
		6	10		4			0			0		
Averages		0.0	0.0		1.7			0.0			0.0		
Cornea		0.0	0.0		0.0			0.0			0.0		
Iris		6.7	11.3		4.0			0.0			0.0		
Conjunctiva		6.7	11.3		5.7			0.0			0.0		
Total													

Iris:

Iris Score = Value x 5

Maximum Score = 10

Conjunctiva:

R = Redness

S = Swelling

D = Discharge

Conjunctival Score =

Cornea:

= Density

A = Area

Corneal Score = D x A x 5

[



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 4:

**Report from Rosner-Hixson Laboratories, Skin Irritation
[IQAC 68122-86-1, 5% dispersion]**



REPORT

Laboratory No. PT72-10

CLIENT: Northern Petrochemical Company of Des Plaines, Illinois.

SAMPLE: Varisoft 475, 5% Aqueous Dispersion. 5% S.D.J. 1PA

OBJECT: To determine the skin irritation potential of the sample in accordance with Federal Hazardous Substances Labeling Act Regulations.

EXPERIMENTAL & RESULTS:

The hair was clipped from the abdomen of six male albino rabbits and two areas of the abdomen approximately ten centimeters apart were designated for application of the patches. A one inch square site on the right side was abraded while a similar site on the left remained unabraded.

One-half milliliter of the sample was placed on the skin under a small square of cotton gauze and maintained in contact with the skin under a larger square of polyethylene film and anchored to the skin with strips of adhesive tape. A square of flannel cloth was then taped around the trunk of the animal to further protect the patches from being dislodged.

After 24 hours the vest and patches were removed and the skin examined for signs of irritation (erythema and/or edema). Examination was made again after 72 hours.

Skin irritation scores are presented in Table 2. See Appendix for Evaluation of Skin Reactions in Primary Irritation Test.

The primary irritation score of 0.83 indicates that the sample is not a primary skin irritant.

SUMMARY & CONCLUSION:

Varisoft 475, 5% Aqueous Dispersion, was tested for primary skin irritation in accordance with Federal Hazardous Substances Labeling Act Regulations.

Application of sample to intact and abraded skin of rabbits produced a primary irritation score of 0.83. Since minimal score of 5 is required for classification as a primary skin irritant this product is not a primary skin irritant.

On the basis of the test, Varisoft 475, 5% aqueous dispersion, is not a primary skin irritant in accordance with Federal Hazardous Substances Labeling Act Regulations. Consequently, precautionary labeling as a skin irritant is not required.

June 6, 1972



ROSNER-HIXSON LABORATORIES

O. F. Hixson

O. F. Hixson, Technical Director

]

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
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TSCA Interagency Testing Committee

Attachment 5:

WARF Institute Report - Skin Irritation
[IQAC 68122-86-1, 5% dispersion]



WARF INSTITUTE, INC.

MADISON, WISCONSIN

211 #3

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any form of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for **Skin Irritation**

Description of Sample **Liquid**

Date Received **11-5-76**

Control Number

Varisoft 475 (5% Active)

Submitted by **Richard M. Egan
Ashland Oil, Inc.
Dublin, OH**

Claimed Content

Results

Skin Irritation Index: 1.75

Method

Please see attached protocol.

Remarks

Signed

by and for the **WARF INSTITUTE, INC.**

Date

December 9, 1976

WARF Institute No.

6111267



WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Oil, Inc.

WARF Institute No. 6111267

Sample Varisoft 475 (5% Active)

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, 1 abraded area, and 1 intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

Animal Number	24 Hours (1)		72 Hours (1)	
	Abraded	Unabraded	Abraded	Unabraded
	Er. Ed.	Er. Ed.	Er. Ed.	Er. Ed.
1	1 - 1	1 - 1	1 - 0	1 - 0
2	1 - 1	1 - 1	1 - 0	1 - 0
3	2 - 1	2 - 1	1 - 0	1 - 0
4	1 - 1	1 - 1	1 - 0	1 - 0
5	2 - 1	2 - 1	1 - 0	1 - 0
6	2 - 1	2 - 1	1 - 0	1 - 0
Score	24-hour	2.50	72-hour	1.00

Primary Skin Irritation Index (2): 1.75

- (1) Score equals sum of erythema and edema readings.
 (2) Skin irritation index equals average of 24 and 72 hour scores.

<u>Erythema and Eschar Formation</u>	<u>Score</u>	<u>Edema Formation</u>	<u>Score</u>
Slight erythema	1	Slight edema (barely perceptible)	1
Defined erythema	2	Defined edema (edges definite rising)	2
Moderate to severe erythema	3	Moderate edema (area raised 1 mm)	3
Severe erythema to slight eschar formation	4	Severe edema (raised more than 1 mm)	4

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Attachment 2: Toxicity Studies for Ashland Oil Company [IQAC 68122-86-1, misc. formulations]	
Attachment 3: Report to Northern Petrochemical Company - Eye Irritation Tests with Eleven Samples in Albino Rabbits [IQAC 68122-86-1, 5% dispersion]	
Attachment 4: Report from Rosner-Hixson Laboratories, Skin Irritation [IQAC 68122-86-1, 5% dispersion]	
Attachment 5: WARF Institute Report - Skin Irritation [IQAC 68122-86-1, 5% dispersion]	
Attachment 6: Dermal Sensitization Study in Guinea Pigs - Raltech Reports Nos. 871605, 871606 & 871607 [IQAC 68122-86-1]	
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Attachment 10: Toxicity Studies for Ashland Oil Company [PEQ 68410-69-5, 4% and 8% dispersions]	

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Attachment 11: Report to Ashland Chemical Company - Acute
Toxicity Studies with Varisoft 222
[PEQ 68410-69-5, 4% dispersion]

Attachment 12: Rosner-Hixson Laboratories Report - Acute LD50
[PEQ 68410-69-5, 18% dispersion]

Attachment 13: WARF Institute Report 7117554 - Primary Eye
Irritation
[PEQ 68410-69-5]

Attachment 14: Rosner-Hixson Laboratories Report - Eye Irritation
[PEQ 68410-69-5, 15% dispersion]

Attachment 15: Rosner-Hixson laboratories Report -
Skin Irritation
[PEQ 68410-69-5, 4% dispersion]

Attachment 16: Report to Northern Petrochemical Company -
Primary Skin Irritation of Eight Samples of Shampoo
in Albino Rabbits
[PEQ 68410-69-5, Full strength and 4% dispersion]

Attachment 17: Bio-Toxicology Laboratories Report -
DOT and FSHA Skin Irritation
[PEQ 68410-69-5]

Attachment 18: Report to Ashland Chemical Company - Skin
Sensitization Test with Varisoft 222 in Albino Guinea Pigs
[PEQ 68410-69-5]

Attachment 19: Delayed Contact Hypersensitivity Study in
Guinea Pigs
[PEQ 68410-69-5]

Attachment 20: Raltech Reports Nos. 816078, 816079, 856938,
856939, 856940, 877521, & 877522 - Skin Sensitization
[PEQ 68410-69-5]

Attachment 21: Biodegradability, Varisoft 222
[PEQ 68410-69-5]

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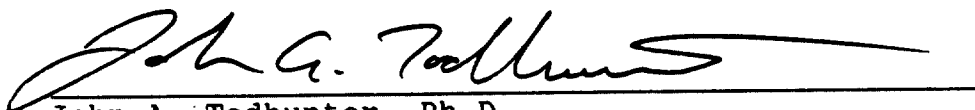
CERTIFICATION OF EXPERT REPORT

The report titled:

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

has been prepared by the undersigned who certifies that any
conclusions drawn in this report are based on a reasonable degree
of scientific certainty and the training and experience of the
undersigned.



John A. Todhunter, Ph.D.
Fellow, American Institute of Chemists
Diplomate, American Board of Toxicology

7-29-93
Date

BACKGROUND

History and Nature of Present Report

In response to the 22nd Report of the TSCA Interagency Testing Committee ("ITC"), members of the Fabric Softener QUATS Steering Committee ("The Committee"), through the auspices of the Chemical Specialties Manufacturers Association, submitted a large number of studies and reports to U.S. EPA.

In response to these submissions, the ITC, via a letter dated February 22, 1993 from John D. Walker, Executive Director, to Jim T. Hill, of CSMA, requested clarification of the relationships among various of the QUATS covered in the aforesaid submissions, justifications for proposing some QUATS as analogs of other QUATS, and various, miscellaneous other points of information.

The Committee engaged its outside consultant, Dr. John A. Todhunter of SRS International Corporation, to review the letter and provide the additional information and/or points of clarification which were requested.

The present report is that prepared by SRS International at the request of the Fabric Softener QUATS Steering Committee.

Scientific Background

The present report deals, in large part, with justification for drawing toxicological analogies between various of the QUATS which are used in fabric softeners.

In this regard, it must be noted that most of the toxicological and ecological effects potential of these compounds is driven by rather non-specific physico-chemical effects as opposed to compound specific biological interactions. For example, the skin or eye irritancy of these compounds is generally similar and is not very sensitive to whether the test substance is EEQ*, an IQAC or a PEQ compound. These effects are produced by defatting of the skin or by a similar defatting of and solubilization of membrane components in the eye and such effects are a physico-chemical effect which is not highly sensitive to differences in structure, so long as any changes in the structure does not abolish the defatting effect. In contrast to such non-specific effects, these compounds do not appear to have any significant

=====

* EEQ is not now, nor has it for many years (if ever) been produced for commercial use in fabric softeners. As a result, there are no studies on EEQ. PEQ is, in any case, an excellent analog. EEG is homologous to the PEQ series and is defined as a PEQ with less than an average of 1.5 ethoxy units in the polyethoxy chain.

ability to bind to specific biological receptors (membrane bound or intracellular) and are at best poorly absorbed from the oral or dermal-routes of exposure. Thus, they have little if any potential for producing toxic effects on humans, domestic animals, or wildlife (including aquatic organisms) by "classical" mechanisms of toxicity. For these reasons, data on a small number of these compounds will be useful in evaluating other compounds, even if they are in another structural class. Of course, for homologous compounds, the analogy will be quite excellent.

For the above reason, and so as to be as responsive to the ITC's interests for each specific QUAT listed in the 22nd ITC report as possible, data was provided in the previous submissions of the Fabric Softener QUATS Steering Committee on compounds which are analagous to the specific compound for which ITC requested information. In some cases the analog is of the same structural class. In some other cases, the analogs were of a different structural class but, due to the non-structure specific mechanisms for production of the effects of interest, were considered to provide appropriate information as to the toxicity potential of the specific compound of interest to ITC. In a few other cases, if any toxicological effect were possible, it would be produced via interactions with specific functional groups which are common between different structural classes of the quaternary ammonium compounds at issue.

In the detailed responses to the ITC's letter of February 22, 1993 which follow, the appropriate structural information is provided for ITC's reference and ease of comparison. Also, the basis upon which specific analogs were proffered is provided.

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 6:

**Dermal Sensitization Study in Guinea Pigs -
Raltech Reports Nos. 871605, 871606 & 871607
[IQAC 68122-86-1]**



ATT #6

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REPORT

MR ROBERT L. HARRISON
SHERREY CHEMICAL COMPANY, INC.
P.O. BOX 646
DUBLIN, OH 43017

RT LAB NO. 871605

ENTERED 06/16/81

REPORTED 09/18/81

VARISET 475: LOT 11384

PURCHASE ORDER NUMBER 021-49378

ENCLOSED: DERMAL SENSITIZATION STUDY IN GUINEA PIGS
(MODIFIED CLOSED PATCH TECHNIQUE) - METHOD, SUMMARY

RAW DATA ATTACHED

SIGNED:

Mary W. Thompson
MARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.



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TEST LAB NUMBER 871605

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VARISOF 475: LOT 1138K

SKIN SENSITIZATION

OBJECTIVE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY POTENTIAL OF A TEST MATERIAL IN GUINEA PIGS.

TEST ANIMAL: TWENTY-FOUR ACCLIMATED GUINEA PIGS, WEIGHING FROM 333 TO 426 G WERE USED FOR THIS STUDY. THE ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA PIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE PLACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL NUMBER AND EAR TAG. THE ANIMALS WERE INDIVIDUALLY HOUSED IN SCREEN-BOTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED ROOMS. ANIMALS WERE PROVIDED CONTINUOUS ACCESS TO PURINA GUINEA PIG CHOW AND WATER THROUGHOUT THE STUDY PERIOD.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 G OF VARISOF 475: LOT 1138K WAS WEIGHED INTO AN Erlenmeyer flask. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRRED USING A STIR PLATE AND A MAGNETIC STIR BAR TO A UNIFORM SUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

TREATMENT: THE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE LEFT SHOULDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED TEST SUBSTANCE ON A WEBER PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER LAM AND SECURED WITH AN OVERLAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED. THE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE RETURNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL OF THREE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE THIRD SENSITIZING DOSE, A CHALLENGE DOSE AT A VOLUME OF 0.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, THE FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WERE ALSO TREATED WITH A CHALLENGE APPLICATION. THE CHALLENGE APPLICATIONS WERE MADE TO A FRESHLY CLIPPED SKIN SITE THAT HAD NOT BEEN PREVIOUSLY TREATED. TWENTY-FOUR HOURS AFTER PRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEST CREAM HAIR REMOVER (WHITEHALL LABORATORIES, INC., NEW YORK). THE DEPILATORY WAS APPLIED ON THE TEST SITES AND SURROUNDING AREAS FOR THIRTY MINUTES. THEN THE DEPILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS DRIED WITH A TOWEL AND RETURNED TO THEIR CAGES.

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PHASE OF THE STUDY. REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED TWO HOURS AFTER DEPIILATION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMALS WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE



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EEB 871605

PAGE 3

LOT 1131K

IZATION (CONTINUED)

STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT
INTERVALS DURING THE STUDY.

1: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.



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LAB NUMBER 571605

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PROJECT 475: LOT 1136K

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIN REACTIONS**

ANIMAL NUMBER	TEST GROUP - MALES			
	SENSITIZING PHASE		CHALLENGE PHASE	
	THREE APPLICATIONS		SINGLE APPLICATION	
	ERYTHEMA		ERYTHEMA	
	AVE.	(HIGH)	AVE.	(HIGH)
64100368	0.0	(0)	0.0	(0)
64100369	0.0	(0)	0.0	(0)
64100370	0.0	(0)	0.0	(0)
64100371	0.0	(0)	0.0	(0)
64100372	0.0	(0)	0.0	(0)
64100373	0.0	(0)	0.0	(0)
64100374	0.0	(0)	0.0	(0)
64100375	0.0	(0)	0.3	(0.5)
64100376	0.0	(0)	0.0	(0)
64100377	0.0	(0)	0.0	(0)

NAIVE CONTROL

64100393	UNTREATED	0.3	(0.5)	0.0	(0)
64100394	UNTREATED	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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TEST LAB NUMBER 871605

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ARISOFT 475: LOT 1136K

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIN REACTIONS** (CONT.):

ANIMAL NUMBER	TEST GROUP - FEMALES							
	SENSITIZING PHASE				CHALLENGE PHASE			
	THREE APPLICATIONS				SINGLE APPLICATION			
	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100419	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100420	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100421	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100422	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100423	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100426	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100429	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100430	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100431	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100432	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
					0.0	(0)	0.0	(0)

NAIVE CONTROL

64100424	UNTREATED	0.0	(0)	0.0	(0)
64100425	UNTREATED	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST READING RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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TEST LAB NUMBER R71605

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VARI-CFT 475: LOT 1138K

SKIN SENSITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY APPEARED NORMAL THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIN REACTIONS TO VARI-CFT 475: LOT 1138K (1.0% W/V AQUEOUS):

ONE MALE ANIMAL (NO. 64100374) AND THREE FEMALE ANIMALS (NOS. 64100420, 64100426 AND 64100430) REACTED TO THE CHALLENGE APPLICATION WITH A VERY FAINT NONCONFLUENT ERYTHEMA AT THE 24 HOUR OBSERVATION.

ONE MALE ANIMAL (NO. 64100376) IN THE NAIVE CONTROL ALSO RESPONDED WITH A VERY FAINT NONCONFLUENT ERYTHEMA AFTER RECEIVING 0.4 ML OF THE 1.0% W/V MIXTURE OF TEST MATERIAL.

BECAUSE THE SKIN REACTION IN THE TREATED ANIMALS DID NOT EXCEED THE MOST SEVERE CONTROL REACTION, THE RESPONSES WERE NOT SUBSTANTIAL ENOUGH TO BE CONSIDERED POSITIVE FOR SENSITIZATION.

CONCLUSION: BECAUSE NO SENSITIZATION WAS DETECTED IN THIS STUDY, THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group

RT No.

871605

Vehicle

sterile

0.9% saline

Test Compound

Varisoft 475

Lot 1138 K



Positive Control Group

NA

Vehicle

NA

Sex ♂

Animal Number								Tech-nician	Date
6410-0368	6410-0369	6410-0370	6410-0371	6410-0372	6410-0373	6410-0374	6410-0375		
420	414	386	426	401	384	342	394	ER	7/22
485	473	438	489	471	463	405	490	NJO	7/29
567	540	500	559	558	538	480	590	JR	8/5
630	603	576	625	622	607	553	676	DL	8/12
705	668	643	668	685	679	582	730	ER	8/19

		Animal Number		
6410-0376	6410-0377		Tech-nician	Date
				198
386	370	Scale Used: K-Tron 4809		
453	443	Scale Used: K-Tron 4809	ER	-
536	525	Scale Used: K-Tron 4809	NJO	7/29
628	586	Scale Used: K-TRON 4809	JR	8/5
690	642	Scale Used: K-Tron 4809	DL	8/12
		Scale Used:	ER	8/19

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisof 475 Lot 1138 K

☒ Positive Control Group NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Technician	Date
6410-0368	6410-0369	6410-0370	6410-0371	6410-0372	6410-0373	6410-0374	6410-0375		
N	N	N	N	N	N	N	N	ER	1981 7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	IR	7/24
N	N	N	N	N	N	N	N	JP	7/25
N	N	N	N	N	N	N	N	IR	7/26
N	N	N	N	N	N	N	N	IR	7/27
N	N	N	N	N	N	N	N	ND	7/28
N	N	N	N	N	N	N	N	ND	7/29
N	N	N	N	N	N	N	N	JP	7/30
N	N	N	N	N	N	N	N	DA	7/31
N	N	N	N	N	N	N	N	CF	8/1
N	N	N	N	N	N	N	N	JP	8/2
N	N	N	N	N	N	N	N	JP	8/3
N	N	N	N	N	N	N	N	dec	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	ND	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile Varisoft 475
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 1138 K

Sex ♂

Animal Number								Tech- nician	Date
6410-0376	6410-0377								1981
N	N							ER	7/22
N	N							ER	7/23
N	N							JK	7/24
N	N							JP	7/25
N	N							JR	7/26
N	N							JP	-
N	N							NDJ	
N	N							NDJ	7/29
N	N							JP	7/30
N	N							DK	7/31
N	N							CA	8/1
N	N							JP	8/2
N	N							JP	8/3
N	N							clw	8/4
N	N							JP	8/5
N	N							NDJ	8/6
N	N							ER	8/7
N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisoft 475
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 1138 K

Sex ♂

Animal Number								Tech- nician	Date
6410- 0368	6410- 0369	6410- 0370	6410- 0371	6410- 0372	6410- 0373	6410- 0374	6410- 0375		
N	N	N	N	N	N	N	N	JP	8/9
N	N	N	N	N	N	N	N	dw	8/10
N	N	N	N	N	N	N	N	IR	8/11
N	N	N	N	N	N	N	N	DR	8/15
N	N	N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	N	N	dw	8/14
N	N	N	N	N	N	N	N	DR	8/15
N	N	N	N	N	N	N	N	DR	8/16
N	N	N	N	N	N	N	N	dw	8/17
N	N	N	N	N	N	N	N	DR	8/18
N	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	dw	8/20
N	N	N	N	N	N	N	N	dw	8/21

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisoft 475
☐ Positive Control Group NA Vehicle NA Room No. 2 Lot 1138 K

Sex ♂

Animal Number								Tech- nician	Date
6410-0376	6410-0377								1981
N	N							JP	8/9
N	N							del	8/10
N	N							JR	8/11
N	N							DR	8/12
N	N							ER	8/13
N	N							del	8/14
N	N							DR	8/15
N	N							DR	8/16
N	N							del	8/17
N	N							DR	8/18
N	N							ER	8/19
N	N							del	8/20
N	N							del	8/21

N - No Visible Abnormalities

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle Sterile 0.9% saline Test Material Varisoft Lot 1138

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0368

Date Animal Received 7/10/81

Date Initiated 7/22

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	EP	WR	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NDP	NDP	7/29
	1.0%	24	0	0	NDP	TP	7/30
		48	0	0	DK	DK	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NDP	NDP	8/10
		48	0	0	EP	EP	8/17
Challenge Dose	0.4	NA	NA	NA	EP	EP	8/19
	1.0%	24	0	0	EP	EP	8/20
		48	0	0	EP	NDP	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 Sterile Test Varisoft

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0369

Date Animal Received 7/10/81

Date Initiated 7/22

Source Dean Daul Sex ♂

Challenge Date 8/10

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	MR	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
	1.0%	24	0	0	NJO	YPO	7/30
		48	0	0	NL	NL	7/31
3	0.4	NA	NA	NA	R	R	8/5
	1.0%	24	0	0	NJO	NJO	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	dcw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline ^{Sterile} Test Mate

☐ Positive Control Group NA Vehicle NA Ani

Date Animal Received 7/10/81

Date

Source Dean Dawl Sex ♂

Challe

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician
1	0.4	NA	NA	NA	JP
	1.0%	24	0	0	ER
		48	0	0	JK
2	0.4	NA	NA	NA	NDD
	1.0%	24	0	0	NTD
		48	0	0	NA
3	0.4	NA	NA	NA	R
	1.0%	24	0	0	NTD
		48	0	0	ER
Challenge Dose	0.4	NA	NA	NA	ER
	1.0%	24	0	0	ER
		48	0	0	ER
		NA	NA	NA	
		24			
		48			

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle Sterile Test Varisoft
0.9% saline Material Lot 1138

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0371

Date Animal Received 7/10/81

Date Initiated 7/22

Source Dean Daul Sex ♂

Challenge Date 8/15

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.4	NA	NA	NA	JR	JR	7/22
	1.0%	24	0	0	ER	MR	7/23
		48	0	0	JR	JK	7/24
2	0.4	NA	NA	NA	NJD	NJD	7/29
	1.0%	24	0	0	NJD	JP	7/30
		48	0	0	DA	DA	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
	1.0%	24	0	0	NJD	NJD	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	da	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline ^{Sterile}

☐ Positive Control Group NA Vehicle NA

Date Animal Received 7/10/81

Source Dean Daul Sex ♂

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician
1	0.4	NA	NA	NA	
	1.0%	24	0	0	
		48	0	0	
2	0.4	NA	NA	NA	
	1.0%	24	0	0	
		48	0	0	
3	0.4	NA	NA	NA	
	1.0%	24	0	0	
		48	0	0	
Challenge Dose	0.4	NA	NA	NA	
	1.0%	24	0	0	
		48	0	0	
		NA	NA	NA	
		24			
		48			

^a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 K Sterile Test Varisoft 475:

☐ Positive Control Group NA Vehicle NA Animal No. 0373 6410-

Date Animal Received 7/22/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	NR	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJP	NJP	7/29
	1.0%	24	0	0	NJO	JP	7/30
		48	0	0	NL	NL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NJO	NJV	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	del	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

⊙ recording error 7/21/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Sterile Test Material Varisoft Lot 1138

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0374

Date Animal Received 7/10/81

Date Initiated 7/22

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.4	NA	NA	NA	R	R	7/22
	1.0%	24	0	0	EL	WR	7/23
		48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
	1.0%	24	0	0	ND	ND	7/30
		48	0	0	ND	ND	7/31
3	0.4	NA	NA	NA	R	R	8/5
	1.0%	24	0	0	ND	ND	8/10
		48	0	0	EL	EL	8/17
Challenge Dose	0.4	NA	NA	NA	EL	EL	8/19
	1.0%	24	0.5	0	EL	EL	8/20
		48	0	0	EL	EL	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Sterile Test Material Varisoft Lot 1138

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0375

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	NWL	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NOD	NOD	7/29
	1.0%	24	0	0	NOD	JP	7/30
		48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NOD	NOD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	dev	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 Sterile Test Varisoft

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0376

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	WR	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NJD	NJD	7/29
	1.0%	24	0	0	NJD	7/30	7/30
		48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NJD	NJD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	ER	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 Sterile Test Varisoft

☐ Positive Control Group NA Vehicle NA Animal No. 0377 6410-

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	IK	7/23
		48	0	0	JK	IK	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
	1.0%	24	0	0	ND	TD	7/30
		48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	ALD	ALD	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	DL	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Comp



Positive Control Group NA Vehicle NA

♀

Animal Number							
6410-0419	6410-0420	6410-0421	6410-0422	6410-0423	6410-0426	6410-0429	6410-0431
393	356	380	378	368	354	336	400
451	399	436	396	427	402	389	480
500	469	490	440	495	468	460	570
565	511	531	481	546	507	489	630
617	547	565	519	605	555	544	680

Animal Number		
6410-0431	6410-0432	
354	365	Scale Used: K-Tron 4809
391	401	Scale Used: K-TRON 4809
442	459	Scale Used: K-TRON 4809
491	501	Scale Used: KTRON 4809
535	560	Scale Used: K-Tron 4809
		Scale Used:

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisoft 475 Lot 1138 K

☒ Positive Control Group NA Vehicle NA Room No. 2

Sex ♀

Animal Number								Tech- nician	Date
6410- 0419	6410- 0420	6410- 0421	6410- 0422	6410- 0423	6410- 0426	6410- 0429	6410- 0430		
N	N	N	N	N	N	N	N	ER	7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	ER	7/24
N	N	N	N	N	N	N	N	JP	7/25
N	N	N	N	N	N	N	N	JR	7/26
N	N	N	N	N	N	N	N	JR	7/27
N	N	N	N	N	N	N	N	N/N	7/28
N	N	N	N	N	N	N	N	N/A	7/29
N	N	N	N	N	N	N	N	TP	7/30
N	N	N	N	N	N	N	N	Dr	7/31
N	N	N	N	N	N	N	N	CS	8/1
N	N	N	N	N	N	N	N	TP	8/2
N	N	N	N	N	N	N	N	TP	8/3
N	N	N	N	N	N	N	N	da	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	N/A	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JR	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisoft 475
☐ Positive Control Group NA Vehicle NA Room No. 2 Lot 1138 K

Sex ♀

Animal Number								Tech- nician	Date
6410-0431	6410-0432								1981
N	N							ER	7/22
N	N							ER	7/23
N	N							JR	7/24
N	N							JR	7/25
N	N							JR	7/26
N	N							JR	7/27
N	N							NDD	7/28
N	N							NDD	7/29
N	N							TP	7/30
N	N							DL	7/31
N	N							CA	8/1
N	N							TP	8/2
N	N							TP	8/3
N	N							del	8/4
N	N							JR	8/5
N	N							NDD	8/6
N	N							ER	8/7
N	N							JR	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 871605

Vehicle

Sterile 0.9% Saline

Test

Material Varisoft 475

Lot # 1138 K

Date Animal Received

5/28/81

Source Dean Daul

Sex

♂

Date Initiated

7/9/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410							1981
0318 [Ⓐ]	0.5	NA	NA	NA	SP	SP	7/9
	5.0%	24	0	0	UD	SP	7/10
		48	0	0	MR	MR	7/11
0318 [Ⓑ]	0.5	NA	NA	NA	SP	SP	7/9
	1.0%	24	0	0	JK	SP	7/10
		48	0	0	MR	MR	7/11
 	 	NA	NA	NA			
		24					
		48					
 	 	NA	NA	NA			
		24					
		48					
 	 	NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

Ⓐ recording error 7/9/81 SP

Dermal Sensitization In Guinea Pigs - Body Weights

☒ Naive ~~True~~ G

☒ ~~Test~~ Group

RT No. 871605

sterile

Vehicle 0.9% saline Test Compound

Varisoft

Lot 1138

NA

Positive Control Group

NA

Vehicle

NA

[illegible]

		Animal Number	Technician	Date
				10
		Scale Used: K-Tron 4809	ER	7/20
		Scale Used: K-TRON 4809	NTD	7/20
		Scale Used: K-TRON 4809	IR	8/5
		Scale Used: K-TRON 4809	DR	8/12
		Scale Used: K-Tron 4809	ER	8/19
		Scale Used:		

NA - Not Applicable

① form change 7/20/81 ee

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Naive ☐ Sterile
 Test Group RT No. 871605 Vehicle 0.9% saline Test Compound Varisoft 475
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 1138 K

Animal Number										Tech- nician	Date
6410-0393	6410-0394	6410-0424	6410-0425								1981
N	N	N	N							ER	7/22
N	N	N	N							ER	7/23
N	N	N	N							IR	7/24
N	N	N	N							JOR	7/25
N	N	N	N							IR	7/26
N	N	N	N							IR	7/27
N	N	N	N							MP	7/28
N	N	N	N							ND	7/29
N	N	N	N							MP	7/30
N	N	N	N							DL	7/31
N	N	N	N							CS	8/1
N	N	N	N							MP	8/2
N	N	N	N							MP	8/3
N	N	N	N							dw	8/4
N	N	N	N							JP	8/5
N	N	N	N							ND	8/6
N	N	N	N							ER	8/7
N	N	N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

① form change 7/20/81 ER

② Recording error
7/24/81
JK

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Naive ☐ Test Group RT No. 871605 Vehicle sterile 0.9% saline Test Compound Varisoft 475 Lot 1138 K
☐ Positive Control Group NA Vehicle NA Room No. 2

Animal Number								Technician	Date
6410-0393	6410-0394	6410-0424	6410-0425						
N	N	N	N					JP	8/9
N	N	N	N					dev	8/11
N	N	N	N					JK	8/11
N	N	N	N					DR	8/12
N	N	N	N					ER	8/13
N	N	N	N					dev	8/14
N	N	N	N					DA	8/15
N	N	N	N					DR	8/16
N	N	N	N					dev	8/17
N	N	N	N					DR	8/18
N	N	N	N					ER	8/1
N	N	N	N					dev	8/20
N	N	N	N					dev	8/21

N - No Visible Abnormalities

NA - Not Applicable

① form change 7/20/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Naive

Group:

RT No. 871605

sterile

Test

Varisoft 47

Vehicle 0.9% saline

Material

Lot 1138K

Date Animal Received 7/10/81

Source Dean Dawi Sex ♂ ♀

Date Initiated 7/22/81

Challenge Date 8/19/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Idema	Technician	Recorded By	Date
6410-							1981
0393	0.4	NA	NA	NA	ER	ER	8/19
♂	1.0%	24	0.5	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0394	0.4	NA	NA	NA	ER	ER	8/19
♂	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0424	0.4	NA	NA	NA	ER	ER	8/19
♀	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0425	0.4	NA	NA	NA	ER	ER	8/19
♀	1.0%	24	0	0	dw	dw	8/20
		48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① form change 7/21/81 ER

② recording error 7/21/81 ER

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 871605

Sterile

Test

Vehicle 0.9% Saline Material Varisett 475

Lot 1138 K

Date Animal Received 5/28/81

Source Dean Dawl Sex ♂

Date Initiated 7/9/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
0277 (A)	0.5	NA	NA	NA	ER	ER	7/7
	1.0%	24	0	0	MR	MR	7/10
		48	0	0	MR	MR	7/17
0277 (B)	0.5	NA	NA	NA	ER	ER	7/7
	5.0%	24	1.0	1.0	ER	ER	7/10
		48	0	0	MR	MR	7/17
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Head
 (A) (B)
 (C) (D)

Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8711005

Vehicle Sterile 0.9% Saline

Test Material

VariSoft 47

LOT 1138K

Date Animal Received 4/10/81

Source Dean Daul

Sex ♂

Date Initiated 6/22/81

Animal No. (Site)	Dose ^a (ml.)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0251 (A)	0.5%	NA	NA	NA	NDV	NDV	6/22/81
	25%	24	1.0	0	JP	JP	6/23
		48	1.0	1.0	NDV	NDV	6/24
0251 (B)	0.5	NA	NA	NA	NDV	NDV	6/22
	50%	24	3.0	3.0	JP	JP	6/23
		48	3.0	3.0	NDV	NDV	6/24
0251 (C)	0.5	NA	NA	NA	NDV	NDV	6/22
	75%	24	3.0	3.0	JP	JP	6/23
		48	3.0	3.0	NDV	NDV	6/24
0251 (D)	0.5	NA	NA	NA	NDV	NDV	6/22
	100%	24	3.0	3.0	JP	JP	6/23
		48	3.0	3.0	NDV	NDV	6/24
		NA	NA	NA			
		24					
		48					

@Recording Error 4/22/81 ME

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Varisoft
 Sterile Test Lot 1138 K

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0421

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	WR	7/23
		48	0	0	JP	JK	7/24
2	0.4	NA	NA	NA	NDD	NDD	7/29
	1.0%	24	0	0	NDD	JP	7/30
		48	0	0	JK	JK	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NDD	NDD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	DAI	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Varisoft 4
lot 1138 K

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0422

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	MR	7/23
		48	0	0	JR	IR	7/24
2	0.4	NA	NA	NA	NJN	NJN	7/29
	1.0%	24	0	0	NJN	7/30	7/30
		48	0	0	NA	NA	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NJN	NJN	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	ER	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 K

Sterile

Test

Varisoft

☐ Positive Control Group NA Vehicle NA Animal No. 0423

6410-

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	MS	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
	1.0%	24	0	0	NJO	TP	7/30
		48	0	0	JK	JK	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NJO	NJO	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	SP	SP	8/19
	1.0%	24	0	0	SP	SP	8/20
		48	0	0	ER	clw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle sterile 0.9% saline Test Material Varisoft 4 Lot 1138 K

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0426

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	MR	7/23
		48	0	0	IR	JK	7/24
2	0.4	NA	NA	NA	NJD	NJD	7/29
	1.0%	24	0	0	NJD	JP	7/30
		48	0	0	NL	NL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NJD	NJD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0.5	0	ER	ER	8/20
		48	0	0	ER	NL	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Lot 1138 K Sterile Test Varisoft 4

☒ Positive Control Group NA Vehicle NA Animal No. 6410-2 02042

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	ML	7/23
		48	0	0	JP	JP	7/24
2	0.4	NA	NA	NA	NOD	NOD	7/29
	1.0%	24	0	0	NOD	JP	7/30
		48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NOD	NOD	8/16
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0 to 0	0	ER	ER	8/20
		48	0	0	ER	DL	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

① recording error 8/20/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline ^{Sterile}

☐ NA Positive Control Group NA Vehicle NA

Date Animal Received 7/10/81

Source Dean Daul Sex ♀

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician
1	0.4	NA	NA	NA	
		24	0	0	
	1.0%	48	0	0	
2	0.4	NA	NA	NA	
		24	0	0	
	1.0%	48	0	0	
3	0.4	NA	NA	NA	
		24	0	0	
	1.0%	48	0	0	
Challenge Dose	0.4	NA	NA	NA	
		24	0.5	0	
	1.0%	48	0	0	
		NA	NA	NA	
		24			
		48			

^a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871605 Vehicle 0.9% saline Material Varisoft 4
Lot 1138 K

☒ Positive Control Group NA Vehicle NA Animal No. 6410-0431

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	JP	JP	7/22
	1.0%	24	0	0	ER	MR	7/23
		48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	NTD	NTD	7/29
	1.0%	24	0	0	NTD	NTD	7/30
		48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
	1.0%	24	0	0	NTD	NTD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	ER	8/20
		48	0	0	ER	den	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GU

☒ Test Group: RT No. 871605 Vehi

☐ NA Positive Control Group NA Vehi

Date Animal Received 7/10/81

Source Dean Daul Sex ♀

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema
1	0.4	NA	NA
	1.0%	24	0
		48	0
2	0.4	NA	NA
	1.0%	24	0
		48	0
3	0.4	NA	NA
	1.0%	24	0
		48	0
Challenge Dose	0.4	NA	NA
	1.0%	24	0
		48	0
		NA	NA
		24	
		48	

a - Dosage applied by technician indicated
NA - Not Applicable



ATT #6

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REPORT

MR ROBERT L. HARRISON
SHARKEY CHEMICAL COMPANY, INC.
P.O. BOX 846
DUBLIN, OH 43017

RT LAB NO. 871606

ENTERED 06/16/81

REPORTED 09/18/81

LABORATORY 475: LOT 1104K

PURCHASE ORDER NUMBER 021-49378

CLOSED: DERMAL SENSITIZATION STUDY IN GUINEA PIGS
(MODIFIED CLOSED PATCH TECHNIQUE) - METHOD, SUMMARY
RAW DATA ATTACHED

SIGNED: *Mary A. Thompson*
MARY A. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.



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NUMBER 271606

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LOT 475: LOT 1104K

SENSITIZATION

PURPOSE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY POTENTIAL OF TEST MATERIAL IN GUINEA PIGS.

TEST ANIMAL: TWENTY-FOUR ACCLIMATED GUINEA PIGS, WEIGHING FROM 324 TO 416 G WERE USED FOR THIS STUDY. THE ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA PIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE PLACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL NUMBER AND EAR TAG. THE ANIMALS WERE INDIVIDUALLY HOUSED IN SCREEN-BOTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED ROOMS. THE ANIMALS WERE PROVIDED CONTINUOUS ACCESS TO PURINA GUINEA PIG CHOW AND WATER THROUGHOUT THE STUDY PERIOD.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 G OF VAPISOFT 475: LOT 1104K WAS WEIGHED INTO AN ERLLENMEYER FLASK. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRRED USING A STIR PLATE AND A MAGNETIC STIR BAR TO A UNIFORM SUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

ADMINISTRATION: ONE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE SHOULDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED TEST SUBSTANCE ON A WEBBIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED. THE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE RETURNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL OF THREE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE THIRD SENSITIZING DOSE, A CHALLENGE DOSE AT A VOLUME OF 0.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, THE FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WERE ALSO TREATED WITH A CHALLENGE APPLICATION. THE CHALLENGE APPLICATIONS WERE MADE TO A FRESHLY CLIPPED SKIN SITE THAT HAD NOT BEEN PREVIOUSLY TREATED. TWENTY-FOUR HOURS AFTER PRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEET CREAM HAIR REMOVER (WHITEHALL LABORATORIES, INC., NEW YORK). THE DEPILATORY WAS APPLIED ON THE TEST SITES AND SURROUNDING AREAS FOR 30 MINUTES. THEN THE DEPILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS DRIED WITH A TOWEL AND RETURNED TO THEIR CAGES.



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LAE NUMBER 871606

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VARISOFT 475; LOT 1104K

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PHASE OF THE STUDY. REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED TWO HOURS AFTER DEPILATION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMALS WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT WEEKLY INTERVALS DURING THE STUDY.

BECAUSE ONE ANIMAL (NO. 64100402) EXHIBITED A POSSIBLE SENSITIZATION RESPONSE TO THE CHALLENGE DOSE, A RECHALLENGE WAS CONDUCTED ON THIS ANIMAL 7 DAYS AFTER THE PRIMARY CHALLENGE. THE SENSITIZED ANIMAL (NO. 64100402, MALE), ALONG WITH 4 NAIVE CONTROL (ONCE CHALLENGED) ANIMALS, WERE TREATED WITH 0.4 ML OF RT # 871605 (VARISOFT 475, LOT 1138K) AND 0.4 ML OF RT # 871607 (VARISOFT 475, LOT 195-136) IN THE SAME MANNER AS FOR THE PRIMARY CHALLENGE PROCEDURE, INCLUDING DEPILATION AND 24 AND 48 HOUR SCORES.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.



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LAB NUMBER: 971606

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CRIS 12 475: 107 1104K

SKIN IDENTIFICATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

BATH ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/28/81

SUMMARY OF SKIN REACTIONS**

TEST GROUP - MALES

ANIMAL NUMBER	SENSITIZING PHASE THREE APPLICATIONS				CHALLENGE PHASE SINGLE APPLICATION			
	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100397	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100399	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100400	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100401	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100402	0.0	(0)	0.0	(0)	0.0	(0)	0.5	(1)
64100403	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100404	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100405	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
100406	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100407	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)

NAIVE CONTROL

64100378	UNTREATED	0.3	(0.5)	0.0	(0)
10380	UNTREATED	0.0	(0)	0.0	(0)

THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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LAB NUMBER R71606-

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CARISOP 475: LOT 1104K

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIG

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/28/81

SUMMARY OF SKIN REACTIONS** (CONT.):

TEST GROUP - FEMALES

ANIMAL NUMBER	SENSITIZING PHASE THREE APPLICATIONS				CHALLENGE PHASE SINGLE APPLICATION			
	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100427	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100447	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100409	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100411	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100412	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100413	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100414	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100415	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
100416	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100443	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)

NAIVE CONTROL

64100410	UNTREATED	0.0	(0)	0.0	(0)
64100408	UNTREATED	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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LAP NUMBER 871606

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VARISOFT 475: LOT 1104K

SKIN SENSITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY APPEARED NORMAL THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIN REACTIONS TO VARISOFT 475: LOT 1104K (1.0% W/V AQUEOUS): ONE MALE ANIMAL (NO. 64100402) RESPONDED TO THE CHALLENGE APPLICATION WITH A SLIGHT EDEMA REACTION AT THE 24 HOUR OBSERVATION. TWO FEMALE ANIMALS (NOS. 6410-0409 AND 64100411) REACTED TO THE CHALLENGE DOSE WITH A VERY FAINT NONCONFLUENT ERYTHEMA AT THE 24 HOUR OBSERVATION.

ONE MALE ANIMAL IN THE NAIVE CONTROL (NO. 64100378) EXHIBITED A VERY FAINT ERYTHEMA REACTION AFTER RECEIVING 0.4 ML OF THE 1.0% W/V MIXTURE OF TEST MATERIAL.

THE SKIN REACTIONS IN THE TWO TREATED FEMALES WERE NOT GREATER THAN THE REACTION SEEN IN THE NAIVE CONTROL ANIMALS AND ARE THEREFORE NOT CONSIDERED SENSITIZATION RESPONSES. THE REACTION OF THE ONE TREATED MALE WAS GREATER THAN THE REACTION SEEN IN THE CONTROL ANIMALS AND INDICATES SENSITIZATION.

BECAUSE ONE ANIMAL (NO. 64100402) DID EXHIBIT A SENSITIZATION RESPONSE TO THE CHALLENGE DOSE, A RECHALLENGE WAS CONDUCTED ON THIS ANIMAL AND FOUR NAIVE CONTROL (ONCE CHALLENGED) ANIMALS SEVEN DAYS FOLLOWING THE PRIMARY CHALLENGE.

FOR THE RECHALLENGE DOSE, THE TEST MATERIALS (VARISOFT 475, LOT 1138K AND VARISOFT 475, LOT 195-136, 1.0% W/V AQUEOUS SUSPENSIONS OF EACH) WERE APPLIED TO ONE TEST SITE EACH ON THE TEST AND NAIVE CONTROL ANIMALS. NONE OF THE ANIMALS RESPONDED TO THE RECHALLENGE DOSE WITH ANY SENSITIZATION REACTION AT EITHER OF THE OBSERVATION PERIODS.

CONCLUSION:

BECAUSE THE INCIDENCE OF A SENSITIZATION RESPONSE OCCURRED IN ONLY 5% OF THE TREATED ANIMALS (1 OF 20), THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

Dermal Sensitization In Guinea Pigs - Body Weights

☒ Test Group RT No. 871606 Vehicle sterile 0.9% saline Test Compound Varisoft 475 Lot 1104K
☐ Positive Control Group NA Vehicle NA

Sex ♂

Animal Number								Tech- nician	Date
6410- 0397	6410- 0399	6410- 0400	6410- 0401	6410- 0402	6410- 0403	6410- 0404	6410- 0405		
402	400	366	357	409	384	416	359	ER	7/22
478	498	432	426	484	460	496	410	ND	7/29
537	579	490	490	562	537	580	473	JK	8/5
623	668	554	538	634	614	686	566	DR	8/12
707	737	597	587	697	696	708	618	ER	8/19

		Animal Number		
6410- 0406	6410- 0407		Tech- nician	Date 1981
387	382	Scale Used: K-Tron 4809	ER	7/22
462	469	Scale Used: K-Tron 4809	ND	7/29
548	534	Scale Used: K-Tron 4809	IR	8/5
637	598	Scale Used: K-Tron 4809	DR	8/12
693	643	Scale Used: K-Tron 4809	ER	8/19
	-	-Scale Used:		

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

Varisoft 475

☒ Test Group RT No. 871606 Vehicle Sterile 0.9% saline Test Compound Lot 1104 K

☐ Positive Control Group. NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Tech- nician	Date 1981
6410- 0397	6410- 0399	6410- 0400	6410- 0401	6410- 0402	6410- 0403	6410- 0404	6410- 0405		
N	N	N	N	N	N	N	N	ER	7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	JP	7/24
N	N	N	N	N	N	N	N	JP	7/25
N	N	N	N	N	N	N	N	JP	7/26
N	N	N	N	N	N	N	N	JP	7/27
N	N	N	N	N	N	N	N	NJD	7/28
N	N	N	N	N	N	N	N	NJD	7/29
N	N	N	N	N	N	N	N	NJD	7/30
N	N	N	N	N	N	N	N	JP	7/31
N	N	N	N	N	N	N	N	JP	8/1
N	N	N	N	N	N	N	N	JP	8/2
N	N	N	N	N	N	N	N	JP	8/3
N	N	N	N	N	N	N	N	CS	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	NJD	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871606 Vehicle 0.9% saline Test Compound Varisoft 475
Sterile Lot 1104 K

☒ Positive Control Group NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Tech- nician	Date 1981
6410- 0406	6410- 0407								
N	N							ER	7/22
N	N							ER	7/23
N	N							ER	7/24
N	N							JP	7/25
N	N							JR	7/26
N	N							JR	7/27
N	N							NA	7/28
N	N							NA	7/29
N	N							NJD	7/30
N	N							ER	7/31
N	N							JP	8/1
N	N							JP	8/2
N	N							JP	8/3
N	N							CS	8/4
N	N							JP	8/5
N	N							NJD	8/6
N	N							ER	8/7
N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

Varisoft 475



Test Group RT No. 871606 Vehicle Sterile 0.9% saline Test Compound Lot 1104 K



Positive Control Group NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Tech- nician	Date 1981
6410- 0397	6410- 0399	6410- 0400	6410- 0401	6410- 0402	6410- 0403	6410- 0404	6410- 0405		
N	N	N	N	N	N	N	N	JP	8/9
N	N	N	N	N	N	N	N	daw	8/10
N	N	N	N	N	N	N	N	IR	8/11
N	N	N	N	N	N	N	N	Dh	8/12
N	N	N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	N	N	CS	8/14
N	N	N	N	N	N	N	N	Dh	8/15
N	N	N	N	N	N	N	N	IR	8/16
N	N	N	N	N	N	N	N	daw	8/17
N	N	N	N	N	N	N	N	Dh	8/18
N	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	daw	8/20
N	N	N	N	N	N	N	N	daw	8/21

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871606 Vehicle 0.9% saline Test Compound Varisoft 475
☒ Positive Control Group NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Technician	Date
6410-0406	6410-0407								
N	N							JR	8/9
N	N							daw	8/10
N	N							JR	8/11
N	N							ER	8/12
N	N							ER	8/13
N	N							ER	8/14
N	N							DR	8/15
N	N							JR	8/16
N	N							daw	8/17
N	N							DR	8/18
N	N							ER	8/19
N	N							daw	8/20
N	N							ER	8/21

N - No Visible Abnormalities

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft+175
Lot 1104 K
6410-
☐ Positive Control Group NA Vehicle NA Animal No. 0397
 Date Animal Received 7/10/81 Date Initiated 7/22/81
 Source Dean Daul Sex ♂ Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	SP	ER	7/22
		24	0	0	MR	ER	7/23
	1.0%	48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	NON	NON	7/29
		24	0	0	NON	NON	7/30
	1.0%	48	0	0	DR	DR	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NON	NON	8/10
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	SP	ER	8/19
		24	0	0	SP	MR	8/20
	1.0%	48	0	0	ER	MR	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable
 ① recording error 8/19/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisof+17 Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0399

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	NR	ER	7/23
	1.0%	48	0	0	IR	JR	7/24
2	0.4	NA	NA	NA	NJD	NJD	7/29
		24	0	0	NJD	NJD	7/30
	1.0%	48	0	0	DL	NR	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	NJD	NJD	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dw	8/20
	1.0%	48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Varisoft 175 Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0400

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	NA	ER	7/23
	1.0%	48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
		24	0	0	ND	ND	7/30
	1.0%	48	0	0	NA	NA	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	NA	NA	8/10
	1.0%	48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	NA	8/20
	1.0%	48	0	0	ER	NA	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft Lot 1104

6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0401

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MP	ER	7/23
	1.0%	48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	0	0	NDV	NDV	7/30
	1.0%	48	0	0	DL	DL	7/30
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NDV	NDV	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dl	8/20
	1.0%	48	0	0	ER	dl	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft Lot 1104
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0402

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	SR	SR	7/22
	1.0%	24	0	0	MR	SR	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NOV	NOV	7/29
	1.0%	24	0	0	NOV	NOV	7/30
		48	0	0	NR	NR	7/31
3	0.4	NA	NA	NA	TR	TR	8/5
	1.0%	24	0	0	NOV	NOV	8/10
		48	0	0	SR	SR	8/17
Challenge Dose	0.4	NA	NA	NA	SR	SR	8/19
	1.0%	24	0	0	SR	NOV	8/20
		48	0	0	SR	NOV	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft + Lot 1104 K

6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0403

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MAK	ER	7/23
	1.0%	48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	0	0	NJO	NJO	7/30
	1.0%	48	0	0	DL	NA	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NJO	NJO	8/10
	1.0%	48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	da	8/20
	1.0%	48	0	0	ER	da	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① recording error 8/20/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft Lot 1104

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0404

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	HR	ER	7/23
	1.0%	48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	0	0	NDV	NDV	7/30
	1.0%	48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	IR	IR	8/5
		24	0	0	NDV	NDV	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dlw	8/20
	1.0%	48	0	0	ER	dlw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft + Lot 1104 K

6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0405

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	SP	SP	7/22
		24	0	0	MR	SP	7/23
	1.0%	48	0	0	JR	IK	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
		24	0	0	ND	ND	7/30
	1.0%	48	0	0	JR	ND	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	ND	ND	8/16
	1.0%	48	0	0	SP	SP	8/17
Challenge Dose	0.4	NA	NA	NA	SP	SP	8/19
		24	0	0	SP	ND	8/20
	1.0%	48	0	0	SP	ND	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft Lot 1104

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0406

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	SP	SP	7/22
	1.0%	24	0	0	MP	SP	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJP	NJP	7/29
	1.0%	24	0	0	NJP	NJP	7/30
		48	0	0	JK	JK	7/31
3	0.4	NA	NA	NA	JT	JT	8/5
	1.0%	24	0	0	NJP	NJP	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	SP	SP	8/19
	1.0%	24	0	0	SP	dw	8/20
		48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Varisoft Lot 1104
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0407

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	WP	ER	7/23
	1.0%	48	0	0	IR	JK	7/24
2	0.4	NA	NA	NA	NXX	NXX	7/29
		24	0	0	NXX	NXX	7/30
	1.0%	48	0	0	IX	IX	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NXX	NXX	8/10
	1.0%	48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	deu	8/20
	1.0%	48	0	0	ER	deu	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group_ RT No.

871606

sterile

Vehicle

0.9% saline

Test Compound

Varisoft 4

Lot 1104 K



Positive Control Group

NA

Vehicle

NA

Sex

♀

Animal Number								Tech- nician	Date
6410- 0427	6410- 0447	6410- 0409	6410- 0411	6410- 0412	6410- 0413	6410- 0414	6410- 0415		
359	357	362	406	340	342	361	360	ER	7/2
415	391	409	477	418	397	416	420	ND	7/2
457	454	462	552	498	440	493	492	JR	8/5
506	505	520	604	562	489	540	564	DR	8/1
550	554	580	663	621	531	596	620	ER	8/19

Animal Number			Tech- nician	Date
6410- 0416	6410- 0443			
385	387	Scale Used: K-Tron 4809	ER	7/22
445	459	Scale Used: K-Tron 4809	ND	7/29
486	439	Scale Used: K-Tron 4809	JR	8/5
566	592	Scale Used: KTRON 4809	DR	8/12
633	653	Scale Used: K-Tron 4809	ER	8/19
	-	- Scale Used:		

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group

RT No. 871606

Sterile

Vehicle 0.9% saline

Test Compound

Varisoft 475

Lot 1104 K



Positive Control Group

NA

Vehicle

NA

Room No.

2

Sex ♀

Animal Number								Tech- nician	Date 1981
6410- 0427	6410- 0447	6410- 0409	6410- 0411	6410- 0412	6410- 0413	6410- 0414	6410- 0415		
N	N	N	N	N	N	N	N	ER	7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	JR	7/24
N	N	N	N	N	N	N	N	JP	7/25
N	N	N	N	N	N	N	N	JR	7/26
N	N	N	N	N	N	N	N	JR	7/27
N	N	N	N	N	N	N	N	NDX	7/29
N	N	N	N	N	N	N	N	NDX	7/29
N	N	N	N	N	N	N	N	NDX	7/30
N	N	N	N	N	N	N	N	DA	7/31
N	N	N	N	N	N	N	N	TP	8/1
N	N	N	N	N	N	N	N	TP	8/2
N	N	N	N	N	N	N	N	TP	8/3
N	N	N	N	N	N	N	N	CS	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	NDX	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 871606 Sterile Vehicle 0.9% saline Test Compound Varisoft 475
Lot 1104 K



Positive Control Group NA Vehicle NA Room No. 2

Sex ♀

Animal Number								Tech- nician	Date
6410- 0416	6410- 0443								
N	N							ER	1981 7/22
N	N							ER	7/23
N	N							IR	7/24
N	N							JP	7/25
N	N							IR	7/26
N	N							IR	7/27
N	N							NDA	7/28
N	N							NDA	7/29
N	N							NDA	7/30
N	N							DR	7/31
N	N							MP	8/1
N	N							MP	8/2
N	N							MP	8/3
N	N							CS	8/4
N	N							JP	8/5
N	N							NDA	8/6
N	N							ER	8/7
N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871606 Vehicle sterile 0.9% saline Test Compound Varisoft 475
☒ Positive Control Group NA Vehicle NA Room No. 2
 Sex ♀ Lot 1104 K

Animal Number								Tech- nician	Date
6410- 0427	6410- 0447	6410- 0409	6410- 0411	6410- 0412	6410- 0413	6410- 0414	6410- 0415		
N	N	N	N	N	N	N	N	JP	8/9
N	N	N	N	N	N	N	N	da	8/10
N	N	N	N	N	N	N	N	K	8/11
N	N	N	N	N	N	N	N	DR	8/12
N	N	N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	N	N	CS	8/14
N	N	N	N	N	N	N	N	DR	8/15
N	N	N	N	N	N	N	N	JR	8/16
N	N	N	N	N	N	N	N	da	8/17
N	N	N	N	N	N	N	N	DR	8/18
N	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	da	8/20
N	N	N	N	N	N	N	N	da	8/21

N - No Visible Abnormalities

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisof+17 Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0427

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	SR	SR	7/22
		24	0	0	MR	SR	7/23
	1.0%	48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NDN	NDN	7/29
		24	0	0	NDN	NDN	7/30
	1.0%	48	0	0	DL	NA	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NDN	NDN	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	SR	SR	8/19
		24	0	0	SR	do	8/20
	1.0%	48	0	0	SR	do	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Varisoft+1 Lot 1104 K

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0447

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Dawl Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MR	ER	7/23
	1.0%	48	0	0	JR	JK	7/24
2	0.4	NA	NA	NA	N/D	N/D	7/29
		24	0	0	N/D	N/D	7/30
	1.0%	48	0	0	N/D	N/D	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	N/D	N/D	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	daw	8/20
	1.0%	48	0	0	ER	daw	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Varisoft 17 Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0409

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MM	ER	7/23
	1.0%	48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
		24	0	0	ND	ND	7/30
	1.0%	48	0	0	DA	DA	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	ND	ND	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0.5	0	ER	MM	8/20
	1.0%	48	0	0	ER	DA	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle Sterile-0.9% saline Test Material Varisoft 97 Lot 1104 K

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0411

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	ER	ER	7/22
	1.0%	24	0	0	WR	ER	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NJD	NJD	7/29
	1.0%	24	0	0	NJD	NJD	7/30
		48	0	0	NJD	NJD	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
	1.0%	24	0	0	NJD	NJD	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0.5	0	ER	ER	8/20
		48	0	0	ER	ER	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisof+17 Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0412

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MR	ER	7/23
	1.0%	48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NOT	NOT	7/29
		24	0	0	NOT	NOT	7/30
	1.0%	48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	NOT	NOT	8/10
	1.0%	48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DL	8/20
	1.0%	48	0	0	ER	DL	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

5 Test Group: RT No. 871606 Vehicle 0.9% saline ^{Sterile} Test Material Varisoft+175
6410- Lot 1104 K

NA Positive Control Group NA Vehicle NA Animal No. 0413

ate Animal Received 7/10/81 Date Initiated 7/22/81
 ource Dean Daul Sex ♀ Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
	0.4	NA	NA	NA	EP	EP	7/22
		24	0	0	WV	EP	7/23
	1.0%	48	0	0	JK	JK	7/24
7	0.4	NA	NA	NA	NJY	NJY	7/29
		24	0	0	NJY	NJY	7/30
	1.0%	48	0	0	NL	DL	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	NJY	NJY	8/6
	1.0%	48	0	0	EP	EP	8/7
Challenge Dose	0.4	NA	NA	NA	EP	EP	8/19
		24	0	0	EP	da	8/20
	1.0%	48	0	0	EP	da	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+175

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0414

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	NR	ER	7/23
	1.0%	48	0	0	IR	IR	7/24
2	0.4	NA	NA	NA	NTO	NTO	7/29
		24	0	0	NTO	NTO	7/30
	1.0%	48	0	0	NA	NA	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	NTO	NTO	8/10
	1.0%	48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dw	8/20
	1.0%	48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft+175

Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Lot 1104 K
6410-

Positive Control Group NA Vehicle NA Animal No. 0415

Animal Received 7/10/81

Date Initiated 7/22/81

Animal Name Dean Daul Sex ♀

Challenge Date 8/19/81

Dosing	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	○	○	WJ	ER	7/23
	1.0%	48	○	○	JK	JK	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	○	○	NDV	NDV	7/30
	1.0%	48	○	○	DK	DK	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	○	○	NDV	NDV	8/6
	1.0%	48	○	○	ER	ER	8/7
4 th Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	○	○	ER	dk	8/20
	1.0%	48	○	○	ER	dk	8/21
		NA	NA	NA			
		24					
		48					

- Dosage applied by technician indicated
- Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+175

☒ Test Group: RT No. 871606 Vehicle Sterile 0.9% saline Test Material Lot 1104 K

6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0416

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.4	NA	NA	NA	ce	ce	7/22
		24	0	0	MR	ER	7/23
	1.0%	48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NOV	NOV	7/29
		24	0	0	NOV	NOV	7/30
	1.0%	48	0	0	NA	NA	7/31
3	0.4	NA	NA	NA	JP	JP	8/5
		24	0	0	NOV	NOV	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dew	8/20
	1.0%	48	0	0	ER	dew	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof+175

☒ Test Group: RT No. 871606 Vehicle 0.9% saline ^{Sterile} Test Material

Lot 1104 K
6410-

☐ Positive Control Group NA Vehicle NA Animal No. 0443

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	WK	EP	7/23
	1.0%	48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	ND	ND	7/29
		24	0	0	ND	ND	7/30
	1.0%	48	0	0	DL	DL	7/31
3	0.4	NA	NA	NA	JR	JR	8/5
		24	0	0	ND	ND	8/6
	1.0%	48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	du	8/20
	1.0%	48	0	0	ER	dal	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

☒ ^① Naive Sterile Varisoft 475
 Test Group RT No. 8711606 Vehicle 0.9% saline Test Compound Lot 1104 K
☐ NA Positive Control Group NA Vehicle NA

Animal Number								Tech- nician	1981 Date
6410- 0378 ♂	6410- 0380 ♂	6410- 0410 ♀	6410- 0408 ♀						
355	366	324	326					ER	7/22
435	446	401	403					NDV	7/29
504	518	463	462					JR	8/5
580	561	506	525					DR	8/12
628	607	559	579					ER	8/19

Animal Number								Tech- nician	1981 Date
								ER	7/22
								NDV	7/29
								JR	8/5
								DR	8/12
								ER	8/19

NA - Not Applicable

① form change 7/21/81 ER

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Naive Sterile Varisoft 475
☒ Test Group RT No. 871606 Vehicle 0.9% saline Test Compound Lot 1104 K
☐ NA Positive Control Group NA Vehicle NA Room No. 2

Animal Number								Tech- nician	Date
0378 ♂	6410- 0380 ♂	6410- 0410 ♀	6410- 0408 ♀						1981
N	N	N	N					ER	7/22
N	N	N	N					ER	7/23
N	N	N	N					JK	7/24
N	N	N	N					JP	7/25
N	N	N	N					JK	7/26
N	N	N	N					JK	7/27
N	N	N	N					N/D	7/28
N	N	N	N					N/D	7/29
N	N	N	N					N/D	7/30
N	N	N	N					Dh	7/31
N	N	N	N					TP	8/1
N	N	N	N					TP	8/2
N	N	N	N					TP	8/3
N	N	N	N					CJ	8/4
N	N	N	N					JP	8/5
N	N	N	N					N/D	8/6
N	N	N	N					ER	8/7
N	N	N	N					JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

① form change 7/21/81 ER

Varisoft 475

NA

N - No Visible Abnormalities

NA - Not Applicable .

① form change 7/21/81 ER

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Naive

Test Group:

RT No. 871606 sterile

Vehicle 0.9% saline

Test

Material

Varisoft 475

Lot 1104 K

Date Animal Received 7/10/81

Source Dean Dawl Sex ♂ ♀

Date Initiated 7/22/81

Challenge Date 8/19/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0378	0.4	NA	NA	NA	ER	ER	8/19
♂	1.0%	24	0.5	0	ER	dcw	8/20
		48	0	0	ER	dcw	8/21
0380	0.4	NA	NA	NA	ER	ER	8/19
♂	1.0%	24	0	0	ER	dcw	8/20
		48	0	0	ER	dcw	8/21
0410	0.4	NA	NA	NA	ER	ER	8/19
♀	1.0%	24	0	0	ER	dcw	8/20
		48	0	0	ER	dcw	8/21
0408	0.4	NA	NA	NA	ER	ER	8/19
♀	1.0%	24	0	0	ER	dcw	8/20
		48	0	0	ER	dcw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① form change 7/21/81 ER

Rechallenge

Dermal Sensitization in Guinea Pigs - Daily Observations Variscott 475 : Lot 1



Test Group RT No. 871605 ^{sterile} Vehicle 0.9% saline Test Compound Varisoff 475: Lot 195-

Positive Control Group NA Vehicle NA Room No. 2

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

head
A
B

Rechallenge

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No.

(A) 871605

Sterile

Vehicle 0.9% saline

Test

(A) Varisoft 475

Lot 1138-K

(B) Varisoft 475

Lot 195-136



Positive Control Group

NA

Vehicle

NA

(1)

Animal No.

Date Animal Received

7/10/81

Date Initiated

8/26/81

Source

Deer-Dawl

Sex

♂

Challenge Date

8/26/81

Animal Sensi- tizing Dose No. No.	(ml) Dose ^a	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6410-	0.4	NA	NA	NA	ER	ER	8/26
0402 (A)	1.0%	24	0	0	ER	ER	8/27
		48	0	0	NDV	ER	8/28
6410-	0.4	NA	NA	NA	ER	ER	8/26
0402 (B)	1.0%	24	0	0	ER	ER	8/27
		48	0	0	NDV	ER	8/28
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

(1) form change 8/25/81 ER

Head
A
B

Rechallenge

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. (A) 871605 Vehicle sterile Test (A) Varisoff 475, Lot 1138K
(B) 871607 Vehicle 0.9% saline Material (B) Varisoff 475, Lot 195-13
☐ Positive Control Group NA Vehicle NA Animal No. 1

Date Animal Received 7/10/81

Date Initiated 8/26/81

Source Dean Daul Sex ♂

Challenge Date 8/26/81

Animal Sensitizing Dose No.	(ml) Dose ^a	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410-0393 (A)	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NOV	ER	8/28
6410-0393 (B)	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NOV	ER	8/28
		NA	NA	NA			
		24					
		48					
6410-0394 (A)	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NOV	ER	8/28
6410-0394 (B)	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NOV	ER	8/28

a - Dosage applied by technician indicated

NA - Not Applicable

① form change 8/25/81 ER

Head
A.
B

Rechallenge

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

① Varisoft 475, Lot 1

☒ Test Group: RT No. ① 871605 Sterile Vehicle 0.9% saline Test ② Varisoft 475, L Material 195-136
② 871607

☒ Positive Control Group NA Vehicle NA ① Animal No.

Date Animal Received 7/10/81

Date Initiated 8/26/81

Source Dean Daul Sex ② ♂ ♀

Re-Challenge Date 8/26/81

Animal Sensitizing Dose No. No.	(ml) Dose ^a	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6410-0424 ①	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NA	ER	8/28
6410-0424 ②	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NA	ER	8/28
 		NA	NA	NA			
		24					
		48					
6410-0425 ①	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NA	ER	8/28
6410-0425 ②	0.4	NA	NA	NA	ER	ER	8/26
		24	0	0	ER	ER	8/27
	1.0%	48	0	0	NA	ER	8/28

a - Dosage applied by technician indicated

NA - Not Applicable

① form change 8/25/81 ER

② recording error 8/25/81 ER

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8716016 Vehicle sterile 0.9% ^{Test} Material Varisoft 475 ⁸ Lot 1104K

Date Animal Received 5/28/81

Source Dean Daul Sex ♂

Date Initiated 7/3/81

Animal No.	Dose ^a	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410-	(ml)						1981
0269	0.5	NA	NA	NA	SP	SP	7/13
	① 0.1%	24	0	0	SP	SP	7/14
		48	0	0	SG	SG	7/15
0269	0.5	NA	NA	NA	SP	SP	7/13
	③ 0.1%	24	0	0	SP	SP	7/14
		48	0	0	SG	SG	7/15
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 871606

Vehicle Sterile 0.9% Saline

Test

Material Varisoft 475
Lot 1104K

Date Animal Received

5/28/81

Source

Dedn Daul

Sex

♂

Date Initiated

7/13/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0324	0.5	NA	NA	NA	SR	SR	7/13
		24	0	0	SR	SR	7/14
(A)	0.1%	48	0	0	SG	SG	7/15
0324	0.5	NA	NA	NA	SR	SR	7/13
		24	0	0	SR	SR	7/14
(B)	0.1%	48	0	0	SG	SG	7/15

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Test Material Varisoft 475: Lot 1104K

Date Animal Received 5/28/81

Source Dear Dawl Sex ♂

Date Initiated 7/9/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0314 (A)	0.5	NA	NA	NA	ER	ER	7/9
	1.0%	24	0	0	NA	ER	7/10
		48	0	0	MR	MR	7/11
0314 (B)	0.5	NA	NA	NA	ER	ER	7/9
	5.0%	24	1.0	1.0	ER	ER	7/10
		48	0	0	MR	MR	7/11
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871606 Vehicle sterile 0.9% saline Material Varisoft 47 Lot 1104 K

Date Animal Received 5/28/81

Source Dean Daul Sex ♂

Date Initiated 7/9/81

Animal No.	Dose ^a	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
0296 (A)	0.5	NA	NA	NA	ER	ER	7/9
	5.0%	24	0	0	MR	MR	7/10
		48	0	0	MR	MR	7/11
0296 (B)	0.5	NA	NA	NA	ER	ER	7/9
	1.0%	24	1.0	1.0	ER	ER	7/10
		48	0	0	MR	MR	7/11
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



AT #6

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REPORT

MR ROBERT L. HARRISON
SHREVE CHEMICAL COMPANY, INC.
P.O. BOX 646
DUBLIN, OH 43017

RT LAB NO. 871607

ENTERED 06/16/81

REPORTED 09/18/81

LABISCT 475: LOT 195-136

PURCHASE ORDER NUMBER 021-49378

ENCLOSED: DERMAL SENSITIZATION STUDY IN GUINEA PIGS
(MODIFIED CLOSED PATCH TECHNIQUE) - METHOD, SUMMARY
RAW DATA ATTACHED

SIGNED: *Gary W. Thompson*.....
GARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY

BY AND FOR RATTECH SCIENTIFIC SERVICES, INC.



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LAB NUMBER 971607-

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VARIOSOF 475: LOT 195-136

SKIN SENSITIZATION

OBJECTIVE: TO DETERMINE THE DELAYED CONTACT HYPERSENSITIVITY POTENTIAL OF A TEST MATERIAL IN GUINEA PIGS.

TEST ANIMAL: TWENTY-FOUR ACCLIMATED GUINEA PIGS, WEIGHING FROM 322 TO 402 G WERE USED FOR THIS STUDY. THE ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TWENTY GUINEA PIGS. AN EQUAL NUMBER OF MALE AND FEMALE ANIMALS WERE PLACED IN EACH GROUP. THE ANIMALS WERE IDENTIFIED BY ANIMAL NUMBER AND EAR TAG. THE ANIMALS WERE INDIVIDUALLY HOUSED IN SCREEN-BOTTOM CAGES IN TEMPERATURE AND HUMIDITY CONTROLLED ROOMS. ANIMALS WERE PROVIDED CONTINUOUS ACCESS TO PURINA GUINEA PIG CHOW AND WATER THROUGHOUT THE STUDY PERIOD.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1.0% WEIGHT/VOLUME MIXTURE, 1.0 G OF VARIOSOF 475: LOT 195-136 WAS WEIGHED INTO AN ERLLENMEYER FLASK. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML. THE MIXTURE WAS THEN STIRRED USING A STIR PLATE AND A MAGNETIC STIR BAR TO A UNIFORM SUSPENSION. THE TEST MATERIAL WAS PREPARED FRESH PRIOR TO EACH APPLICATION.

TREATMENT: THE DAY BEFORE EACH APPLICATION THE HAIR WAS REMOVED FROM THE LEFT SHOULDER OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.4 ML OF THE FRESHLY PREPARED TEST SUBSTANCE ON A MEBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED. THE TEST MATERIAL WAS REMOVED BY A GENTLE RINSE WITH WARM WATER BEFORE RETURNING THE ANIMALS TO THEIR CAGES.

THE ANIMALS RECEIVED ONE APPLICATION PER WEEK FOR THREE WEEKS FOR A TOTAL OF THREE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE THIRD SENSITIZING DOSE, A CHALLENGE DOSE AT A VOLUME OF 0.4 ML WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, THE FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WERE ALSO TREATED WITH A CHALLENGE APPLICATION. THE CHALLENGE APPLICATIONS WERE MADE TO A FRESHLY CLIPPED SKIN SITE THAT HAD NOT BEEN PREVIOUSLY TREATED. TWENTY-FOUR HOURS AFTER PRIMARY CHALLENGE, THE ANIMALS WERE DEPILATED WITH NEEET CREAM HAIR REMOVER (WHITEHALL LABORATORIES, INC., NEW YORK). THE DEPILATORY WAS APPLIED ON THE TEST SITES AND SURROUNDING AREAS FOR 30 MINUTES. THEN THE DEPILATORY WAS THOROUGHLY WASHED OFF WITH WARM WATER, THE ANIMALS DRIED WITH A TOWEL AND RETURNED TO THEIR CAGES.



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LAB NUMBER 671607-

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LABS 157-475: 101 195-131

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION DURING THE SENSITIZING PHASE OF THE STUDY. REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED TWO HOURS AFTER DEPILOTION AND 24 HOURS LATER (48 HOUR SCORES). THE ANIMALS WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT WEEKLY INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.



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LAB NUMBER: 71607

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CHARISANT 475: LOT 195-136

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81

DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIN REACTIONS**

TEST GROUP - MALES

ANIMAL NUMBER	SENSITIZING PHASE THREE APPLICATIONS				CHALLENGE PHASE SINGLE APPLICATION			
	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100383	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100384	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100385	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)
64100387	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100388	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100389	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100390	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100391	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100392	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)

NAIVE CONTROL

64100382	UNTREATED	0.0	(0)	0.0	(0)
64100398	UNTREATED	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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TEST LAB NUMBER: R7160Z

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VARIATION 475: LOT 195-136

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN LAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 7/10/81

DATE TEST STARTED: 7/22/81 DATE TEST COMPLETED: 8/21/81

SUMMARY OF SKIN REACTIONS** (CONT.):

ANIMAL NUMBER	TEST GROUP - FEMALES							
	SENSITIZING PHASE				CHALLENGE PHASE			
	THREE APPLICATIONS				SINGLE APPLICATION			
	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100433	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100434	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100435	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100436	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100437	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100438	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100439	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100440	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100441	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100442	0.0	(0)	0.0	(0)	0.3	(0.5)	0.0	(0)

NAIVE CONTROL

64100445	UNTREATED	0.0	(0)	0.0	(0)
64100446	UNTREATED	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE SIX OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE TEST SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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LAB NUMBER 971607-

PAGE 6

VARICT 475: LOT 195-136

SKIN SENSITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY APPEARED NORMAL THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

SKIN REACTIONS TO VARICT 475: LOT 195-136 (1.0% W/V AQUEOUS):

ONE MALE (NO. 64100315) AND ONE FEMALE (NO. 64100442) REACTED TO THE CHALLENGE APPLICATION WITH A VERY FAINT NONCONFLUENT ERYTHEMA AT THE 24 HOUR OBSERVATION. BOTH OF THE RESPONSES WERE NOT SUBSTANTIAL ENOUGH TO BE CONSIDERED POSITIVE FOR SENSITIZATION.

CONCLUSION:

BECAUSE NO SENSITIZATION WAS DETECTED IN THIS STUDY, THIS TEST MATERIAL IS NOT CONSIDERED A STRONG SKIN SENSITIZER.

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 871607

sterile

Vehicle 0.9% saline

Test Compound Varisoft 475



Positive Control Group NA

Vehicle NA

Lot 195-130

Sex ♂

Animal Number								Technician	Date
6410-0383	6410-0384	6410-0385	6410-0387	6410-0388	6410-0395	6410-0390	6410-0396		
359	383	379	368	373	398	402	398	ER	7/22
444	437	403	413	453	447	493	4107	NJM	7/20
528	506	540	489	488	520	573	539	JR	8/5
600	556	606	① 544	532	581	655	598	DL	8/12
669	617	665	599	565	631	706	648	ER	8/19

Animal Number			Technician	Date
6410-0391	6410-0392			
391	393	Scale Used: K-Tron 4809	ER	7/22
481	493	Scale Used: K-TRON 4809	JP	7/29
553	558	Scale Used: K-TRON 4809	JR	8/5
642	633	Scale Used: K-TRON 4809	DL	8/12
719	700	Scale Used: K-TRON 4809	ER	8/19
		Scale Used:		

NA - Not Applicable

① Recording error 8/12/81 DL

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 871607 Vehicle sterile Test Compound Varisoff 475:



Positive Control Group NA Vehicle NA Room No. 2

Sex ♂

Animal Number								Tech- nician	Date
6410- 0383	6410- 0384	6410- 0385	6410- 0387	6410- 0388	6410- 0395	6410- 0390	6410- 0396		
									1981
N	N	N	N	N	N	N	N	ER	7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	JR	7/24
N	N	N	N	N	N	N	N	JR	7/25
N	N	N	N	N	N	N	N	JR	7/26
N	N	N	N	N	N	N	N	JR	7/27
N	N	N	N	N	N	N	N	NJD	7/28
N	N	N	N	N	N	N	N	NJD	7/29
N	N	N	N	N	N	N	N	MP	7/30
N	N	N	N	N	N	N	N	NJD	7/31
N	N	N	N	N	N	N	N	MP	8/1
N	N	N	N	N	N	N	N	MP	8/2
N	N	N	N	N	N	N	N	MP	8/3
N	N	N	N	N	N	N	N	W	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	NJD	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475 :
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 195-136

Sex ♂

Animal Number								Technician	Date
6410-0391	6410-0392								
N	N							ER	7/22
N	N							ER	7/23
N	N							JR	7/24
N	N							JR	7/25
N	N							JR	7/26
N	N							IR	7/27
N	N							NDA	7/28
N	N							NDA	7/29
N	N							TP	7/30
N	N							NDA	7/31
N	N							TP	8/1
N	N							TP	8/2
N	N							TP	8/3
N	N							ED	8/4
N	N							JP	8/5
N	N -							NDA	8/6
N	N							ER	8/7
N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475:

☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 195-136

Sex ♂

Animal Number								Tech- nician	Date 1981
6410- 0383	6410- 0384	6410- 0385	6410- 0387	6410- 0388	6410- 0395	6410- 0390	6410- 0396		
N	N	N	N	N	N	N	N	JP	8/9
N	N	N	N	N	N	N	N	do	8/10
N	N	N	N	N	N	N	N	IR	8/11
N	N	N	N	N	N	N	N	IR	8/12
N	N	N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	N	N	do	8/14
N	N	N	N	N	N	N	N	IR	8/15
N	N	N	N	N	N	N	N	do	8/16
N	N	N	N	N	N	N	N	do	8/17
N	N	N	N	N	N	N	N	IR	8/18
N	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	do	8/20
N	N	N	N	N	N	N	N	ER	8/21

N - No Visible Abnormalities

NA - Not Applicable

① Recording Error do 8/14/81
④ Recording Error do 8/17/81

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871607 Vehicle 0.9% saline Sterile Test Compound Varisoft 475 :
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 195-136

Sex ♂

Animal Number								Tech- nician	Date
6410-0391	6410-0392								1981
N	N							JP	8/9
N	N							WR	8/10
N	N							JR	8/11
N	N							Dh	8/12
N	N							ER	8/13
N	N							dew	8/14
N	N							Lh	8/15
N	N							WR JR	8/16
N	N							dew	8/17
N	N							Dh	8/18
N	N							ER	8/19
N	N							dew	8/20
N	N							ER	8/21

N - No Visible Abnormalities

NA - Not Applicable

① Recording error 8/14/81
 ② Recording error 8/17/81
 ③ Recording error 8/21/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 475
 Lot 195-13

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0383

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	0	0	MR	ER	7/23
		48	0	0	R	JR	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	0	0	rr	rr	7/30
		48	0	0	NJO	NJO	7/31
3	0.4	NA	NA	NA	DL	DL	8/5
		24	0	0	NJO	NJO	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-1
6410

☐ Positive Control Group NA Vehicle NA Animal No. 0384

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	R	R	7/22
		24	0	0	DR	ER	7/23
		48	0	0	JR	IR	7/24
2	0.4	NA	NA	NA	NJV	NJV	7/29
		24	0	0	TR	TR	7/30
		48	0	0	NDA	NDA	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	NDA	NDA	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DA	8/20
		48	0	0	ER	DA	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoff 475:
 Lot 195-136
 6410-
 ive Control Group NA Vehicle NA Animal No. 0385

Received 7/10/81
nDaul Sex ♂

Date Initiated 7/22/81
 Challenge Date 8/19/81

Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
						1981
0.4	NA	NA	NA	JP	ER	7/22
	24	0	0	WAK	ER	7/23
	48	0	0	IK	IK	7/24
0.4	NA	NA	NA	NJO	NJO	7/29
	24	0	0	mp	mp	7/30
	48	0	0	NJO	NJO	7/31
0.4	NA	NA	NA	DR	DR	8/5
	24	0	0	NJO	NJO	8/6
	48	0	0	ER	ER	8/7
0.4	NA	NA	NA	ER	ER	8/19
	24	0.5	0	ER	daw	8/20
	48	0	0	ER	daw	8/21
	NA	NA	NA			
	24					
	48					

^a applied by technician indicated
 applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 475
 Lot 195-13

☒ Positive Control Group NA Vehicle NA Animal No. 6410-0387

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	0	0	MR	ER	7/23
		48	0	0	JK	JP	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NJO	NJO	7/31
3	0.4	NA	NA	NA	Dr	NA	8/5
		24	0	0	NJO	NJO	8/7
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dr	8/20
		48	0	0	ER	dr	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: RT No: 871607 Vehicle sterile 0.9% saline Test Material Varisoft 475:
 Lot 195-136

Positive Control Group NA Vehicle NA Animal No. 6410-0388

Animal Received 7/10/81

Date Initiated 7/22/81

cc Dean Daul Sex ♂

Challenge Date 8/19/81

singing No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	0	0	MR	ER	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NJV	NJV	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NJV	NJV	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	NJV	NJV	8/11
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	den	8/20
		48	0	0	ER	dal	8/21
		NA	NA	NA			
		24					
		48					

- Dosage applied by technician indicated
- Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisort 475
 Lot 195-130

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0395

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	○	○	IMK	EP	7/23
		48	○	○	JK	IK	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	○	○	TP	TP	7/30
		48	○	○	NJO	NJO	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	○	○	NJO	NJO	8/6
		48	○	○	EP	EP	8/7
Challenge Dose	0.4	NA	NA	NA	EP	EP	8/19
		24	○	○	EP	EP	8/20
		48	○	○	EP	DAJ	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
Lot 195-13

☒ Positive Control Group NA Vehicle NA Animal No. 6410-0390

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	0	0	WR	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NTD	NTD	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NTD	NTD	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	NTD	NTD	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DA	8/20
		48	0	0	ER	DA	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 471

Lot 195-13

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0396

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♂

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.4	NA	NA	NA	JP	JP	7/22
		24	0	0	MP	EP	7/23
		48	0	0	JP	JP	7/24
2	0.4	NA	NA	NA	NXN	NXN	7/29
		24	0	0	MP	MP	7/30
		48	0	0	NXN	NXN	7/31
3	0.4	NA	NA	NA	DL	DL	8/5
		24	0	0	NXN	NXN	8/6
		48	0	0	EP	EP	8/7
Challenge Dose	0.4	NA	NA	NA	EP	EP	8/19
		24	0	0	EP	DL	8/20
		48	0	0	EP	DL	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

RMAL SENSITIZATION STUDY IN GUINEA PIGS

RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 475:
 Lot 195-136

Control Group NA Vehicle NA Animal No. 6410-0391

dated 7/10/81

Date Initiated 7/22/81

Sex ♂

Challenge Date 8/19/81

	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
						1981
1	NA	NA	NA	JP	JP	7/22
	24	0	0	AMP	ER	7/23
	48	0	0	IK	IK	7/24
4	NA	NA	NA	NDV	NDV	7/29
	24	0	0	NDV	NDV	7/30
	48	0	0	NDV	NDV	7/31
4	NA	NA	NA	DL	DL	8/5
	24	0	0	NDV	NDV	8/10
	48	0	0	ER	ER	8/17
4	NA	NA	NA	ER	ER	8/19
	24	0	0	ER	dlw	8/20
	48	0	0	ER	del	8/21
	NA	NA	NA			
	24					
	48					

led by technician indicated
 ple

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 475
 Lot 195-130
☒ Positive Control Group NA Vehicle NA Animal No. 6410-0392

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Paul Sex ♂

Challenge Date 8/19/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	JP	JP	7/21
		24	0	0	MP	ER	7/23
		48	0	0	IK	IK	7/24
2	0.4	NA	NA	NA	NDX	NDX	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NDX	NDX	7/31
3	0.4	NA	NA	NA	DL	NA	8/5
		24	0	0	NDX	NDX	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	da	8/20
		48	0	0	ER	da	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475
 Positive Control Group NA Vehicle NA Lot 195-136

ex ♀

Animal Number								Tech- nician	Date 1981
10-33	6410-0434	6410-0435	6410-0436	6410-0437	6410-0438	6410-0439	6410-0440		
25	359	360	380	380	358	374	368	ER	7/22
59	408	427	424	444	400	425	432	JP	7/29
20	451	492	502	497	436	483	504	JK	8/5
72	495	539	554	555	486	537	566	DK	8/12
13	533	596	605	590	523	574	623	ER	8/19

Animal Number			Tech- nician	Date 1981
10-141	6410-0442			
73	362	Scale Used: K-Tron 4809	ER	7/22
	405	Scale Used: K-Tron 4809	JP	7/29
16	434	Scale Used: K-Tron 4809	JK	8/5
57	471	Scale Used: KTRON 4809	DK	8/12
10	527	Scale Used: K-Tron 4809	ER	8/19
		Scale Used:		

Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475:
☒ Positive Control Group NA Vehicle NA Room No. 2 Lot 195-136

Animal Number								Tech- nician	Date 1981
6410- 0433	6410- 0434	6410- 0435	6410- 0436	6410- 0437	6410- 0438	6410- 0439	6410- 0440		
N	N	N	N	N	N	N	N	ER	7/22
N	N	N	N	N	N	N	N	ER	7/23
N	N	N	N	N	N	N	N	JK	7/24
N	N	N	N	N	N	N	N	JP	7/25
N	N	N	N	N	N	N	N	JK	7/26
N	N	N	N	N	N	N	N	JK	7/27
N	N	N	N	N	N	N	N	NDP	7/28
N	N	N	N	N	N	N	N	NDP	7/29
N	N	N	N	N	N	N	N	YP	7/30
N	N	N	N	N	N	N	N	NDP	7/31
N	N	N	N	N	N	N	N	YP	8/1
N	N	N	N	N	N	N	N	YP	8/2
N	N	N	N	N	N	N	N	YP	8/3
N	N	N	N	N	N	N	N	CD	8/4
N	N	N	N	N	N	N	N	JP	8/5
N	N	N	N	N	N	N	N	NDP	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475 :
 Lot 195-136



Positive Control Group NA Vehicle NA Room No. 2

♀

Animal Number								Tech- nician	Date 1981
6410- 0441	6410- 0442								
N	N							ER	7/22
N	N							ER	7/23
N	N							JK	7/24
N	N							JR	7/25
N	N							JK	7/26
N	N							JK	7/27
N	N							NJA	7/28
N	N							NJA	7/29
N	N							TP	7/30
N	N							NJA	7/31
N	N							TP	8/1
N	N							TP	8/2
N	N							TP	8/3
N	N							CS	8/4
N	N							JP	8/5
N	N							NJA	8/6
N	N							ER	8/7
N	N							JP	8/8

N - No Visible Abnormalities

NA - Not Applicable

3 sterilization in Guinea Pigs - Daily Observations

RT No. 871607 Vehicle 0.99% saline Test Compound Varissoft 475:

Control Group NA Vehicle NA Room No. 2 Lot 195-136

Animal Number						Tech- nician	Date
6410- 0435	6410- 0436	6410- 0437	6410- 0438	6410- 0439	6410- 0440 0440		
							1981
N	N	N	N	N	N	JP	8/9
N	N	N	N	N	N	dew	8/10
N	N	N	N	N	N	IK	8/11
N	N	N	N	N	N	DK	8/12
N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	dew	8/14
N	N	N	N	N	N	DK	8/15
N	N	N	N	N	N	DK	8/16
N	N	N	N	N	N	dew	8/17
N	N	N	N	N	N	DK	8/18
N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	dew	8/20
N	N	N	N	N	N	dew	8/21

N - No Visible Abnormalities

NA - Not Applicable

① recording error 7/21/81 ER

② recording error 8/17/81 dew

Dermal Sensitization in Guinea Pigs - Daily Observations

Positive Control Group NA Vehicle NA Room No. 2 Lot 195-136

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

① According to your slides doc

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0433

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MP	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJN	NJN	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NJN	NJN	7/31
3	0.4	NA	NA	NA	DL	NA	8/5
		24	0	0	NJN	NJN	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	dcw	8/20
		48	0	0	ER	dcw	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle 0.9% saline ^{Sterile} Test Material Varisoft 47
 Lot 195-136

☒ Positive Control Group NA Vehicle NA Animal No. 6410-0434

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.4	NA	NA	NA	EP	EP	7/22
		24	0	0	IK	EP	7/23
		48	0	0	IK	K	7/24
2	0.4	NA	NA	NA	NTD	NTD	7/29
		24	0	0	TD	TD	7/30
		48	0	0	NTD	NTD	7/31
3	0.4	NA	NA	NA	DL	DL	8/5
		24	0	0	NTD	NTD	8/6
		48	0	0	EP	EP	8/7
Challenge Dose	0.4	NA	NA	NA	EP	EP	8/19
		24	0	0	EP	DL	8/20
		48	0	0	EP	DL	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0435

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	SP	SP	7/22
		24	0	0	NR	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NDN	NDN	7/29
		24	0	0	MP	MP	7/30
		48	0	0	NDN	NDN	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	NDN	NDN	8/5
		48	0	0	ER	ER	8/5
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DR	8/20
		48	0	0	ER	DR	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 4
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0436

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	SR	ER	7/22
		24	0	0	ML	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NDV	NDV	7/31
3	0.4	NA	NA	NA	JK	NA	8/5
		24	0	0	NDV	NDV	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	NDV	8/20
		48	0	0	ER	NDV	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle 0.9% saline ^{Sterile} Test Material Varisoft 41
 Lot 195-136
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0437
 Date Animal Received 7/10/81 Date Initiated 7/22/81
 Source Dean Daul Sex ♀ Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.4	NA	NA	NA	SP	SP	7/22
		24	0	0	WJL	SP	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NDD	NDD	7/29
		24	0	0	TYP	TYP	7/30
		48	0	0	NDD	NDD	7/31
3	0.4	NA	NA	NA	DH	DH	8/5
		24	0	0	NDD	NDD	8/12
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	SP	SP	8/19
		24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0438

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MR	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	0	0	TY	TY	7/30
		48	0	0	NJO	NJO	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	NJO	NJO	8/6
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	AN	8/20
		48	0	0	ER	AN	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0439

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	WAK	ER	7/23
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NJO	NJO	7/29
		24	0	0	TP	TP	7/30
		48	0	0	NJO	NJO	7/31
3	0.4	NA	NA	NA	DR	DR	8/5
		24	0	0	ALDI	ALDI	8/10
		48	0	0	ER	ER	8/17
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	don	8/20
		48	0	0	ER	don	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0440

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	ER	ER	1981
		24	0	0	WK	ER	7/22
		48	0	0	JK	JK	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	0	0	TPP	TPP	7/30
		48	0	0	NDV	NDV	7/31
3	0.4	NA	NA	NA	DL	DL	8/5
		24	0	0	NDV	NDV	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	da	8/20
		48	0	0	ER	da	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle 0.9% saline ^{Sterile} Test Material Varisoft 47
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0441

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MR	ER	7/23
		48	0	0	JR	JR	7/24
2	0.4	NA	NA	NA	NDP	NDP	7/29
		24	0	0	MP	MP	7/30
		48	0	0	NDP	NDP	7/31
3	0.4	NA	NA	NA	DL	DL	8/5
		24	0	0	NDP	NDP	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DL	8/20
		48	0	0	ER	DL	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Test Material Varisoft 471
 Lot 195-136

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0442

Date Animal Received 7/10/81

Date Initiated 7/22/81

Source Dean Daul Sex ♀

Challenge Date 8/19/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.4	NA	NA	NA	ER	ER	7/22
		24	0	0	MM	ER	7/23
		48	0	0	IR	JK	7/24
2	0.4	NA	NA	NA	NDV	NDV	7/29
		24	0	0	MP	MP	7/30
		48	0	0	NDV	NDV	7/31
3	0.4	NA	NA	NA	DR	NA	8/5
		24	0	0	NDV	NDV	8/6
		48	0	0	ER	ER	8/7
Challenge Dose	0.4	NA	NA	NA	ER	ER	8/19
		24	0	0	ER	DD	8/20
		48	0.5	0	ER	DD	8/21
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights



Naive

①

Test Group - RT No. 871607 Vehicle ^{sterile} 0.9% saline Test Compound Varisoft 475 Lot 195-136



Positive Control Group NA Vehicle NA

Animal Number								Tech-nician	Date
6410-0382	6410-0398	6410-0445	6410-0446						
375	322	368	379					ER	7/22
460	419	456	442					JP	7/29
548	490	524	496					JR	8/5
604	551	595	532					DL	8/12
692	601	651	566					ER	8/19

Animal Number								Tech-nician	Date
		Scale Used: K-Tron 4809						ER	7/22
		Scale Used: K-Tron 4809						JP	7/29
		Scale Used: K-Tron 4809						JR	8/5
		Scale Used: KTRON 4809						DL	8/12
		Scale Used: K-Tron 4809						ER	8/19
		- Scale Used:							

NA - Not Applicable

① form change 7/22/81 ER

Dermal-Sensitization in Guinea Pigs - Daily Observations

☒ Naive Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 4750
 Lot 195-136
☐ NA Positive Control Group NA Vehicle NA Room No. 2

Animal Number										Tech- nician	Date 1981
6410- 0382 ♂	6410- 0398 ♂	6410- 0445 ♀	6410- 0446 ♀								
N	N	N	N							ER	7/22
N	N	N	N							ER	7/23
N	N	N	N							JR	7/24
N	N	N	N							JP	7/25
N	N	N	N							JR	7/26
N	N	N	N							JR	7/27
N	N	N	N							NJD	7/28
N	N	N	N							NJD	7/29
N	N	N	N							YP	7/30
N	N	N	N							YP	7/31
N	N	N	N							YP	8/1
N	N	N	N							YP	8/2
N	N	N	N							YP	8/3
N	N	N	N							CA	8/4
N	N	N	N							JP	8/5
N	N	N	N							NJD	8/6
N	N	N	N							ER	8/7
N	N	N	N							JP	8/8

① form change 7/20/81 ER

N - No Visible Abnormalities

NA - Not Applicable

Dermal-Sensitization in Guinea Pigs - Daily Observations

☒ Naive ☐ Test Group RT No. 871607 Vehicle sterile 0.9% saline Test Compound Varisoft 475 Lot 195-136
☒ NA Positive Control Group NA Vehicle NA Room No. 2

Animal Number										Tech- nician	Date 1981
6410- 0382 ♂	6410- 0398 ♂	6410- 0445 ♀	6410- 0446 ♀								
N	N	N	N							JP	8/9
N	N	N	N							daw	8/10
N	N	N	N							JR	8/11
N	N	N	N							DR	8/12
N	N	N	N							ER	8/13
N	N	N	N							daw	8/14
N	N	N	N							DR	8/15
N	N	N	N							daw ①	8/16
N	N	N	N							daw	8/17
N	N	N	N							DR	8/18
N	N	N	N							ER	8/19
N	N	N	N							daw	8/20
N	N	N	N							daw	8/21
N	N	N	N ②							daw ②	8/22 ②

① form change 7/20/81 ER

N - No Visible Abnormalities

NA - Not Applicable

① ~~RECORDING~~ 8/17/81 daw
 ② ~~RECORDING~~ 8/21/81 daw

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Naive
Test Group: 0

RT No. 871607

sterile

Test

Vehicle 0.9% saline

Material

Varisoft 475

Lot 195-136

Date Animal Received 7/10/81

Source Dean Dawl Sex ♂ ♀

Date Initiated 7/22/81

Challenge Date 8/19/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410-							1981
0382 ♂	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0398 ♂	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0445 ♀	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
0446 ♀	0.4	NA	NA	NA	ER	ER	8/19
	1.0%	24	0	0	ER	dw	8/20
		48	0	0	ER	dw	8/21
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

① form change 7/21/81 ER

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline ^{Test} Material Varisoft 475: Lot 195-136

Date Animal Received 5/28/81

Source Dean Daul Sex ♂

Date Initiated 7/9/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0295 (A)	0.5	NA	NA	NA	ER	ER	7/9
	1.0%	24	0	0	NR	NR	7/10
		48	0	0	NR	NR	7/11
0295 (B)	0.5	NA	NA	NA	ER	ER	7/9
	5.0%	24	1.0	1.0	NR	NR	7/10
		48	1.0	0	NR	NR	7/11
 	 	NA	NA	NA			
		24					
		48					
 	 	NA	NA	NA			
		24					
		48					
 	 	NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 871607 Vehicle sterile 0.9% saline Material Varisoft 475:
Test
Lot 195-136

Date Animal Received 5/28/81

Source Dean Daul Sex ♂

Date Initiated 7/9/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0272 (A)	0.5	NA	NA	NA	ER	ER	7/9
		24	0	0	ADN	EP	7/10
	5.0%	48	0	0	MR	MR	7/11
0272 (B)	0.5	NA	NA	NA	ER	ER	7/9
		24	0	0	ADN	EP	7/10
	1.0%	48	0	0	MR	MR	7/11
 	 	NA	NA	NA	 	 	
	 	24	 	 	 	 	
	 	48	 	 	 	 	
 	 	NA	NA	NA	 	 	
	 	24	 	 	 	 	
	 	48	 	 	 	 	
 	 	NA	NA	NA	 	 	
	 	24	 	 	 	 	
	 	48	 	 	 	 	

a - Dosage applied by technician indicated

NA - Not Applicable

Head
 (A) / (B)
 (C) / (D)

Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No.

871607

Sterile 0.9% Test

Vehicle

Varisof 1%

Material

Varisof + 475

195-136
Saline

LOT 1138K

Date Animal Received

4/10/81

Source

Dean Paul

Sex

♂

Date Initiated

6/22/81

Animal No. <u>Site</u>	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0179 (A)	0.5	NA	NA	NA	NDA	NDA	6/22
	25%	24	1.0	1.0	NDA	NDA	6/23
		48	2.0	2.0	NDA	NDA	6/24
0179 (B)	0.5	NA	NA	NA	NDA	NDA	6/22
	50%	24	1.0	1.0	NDA	NDA	6/23
		48	2.0	2.0	NDA	NDA	6/24
0179 (C)	0.5	NA	NA	NA	NDA	NDA	6/22
	75%	24	2.0	1.0	NDA	NDA	6/23
		48	2.0	2.0	NDA	NDA	6/24
0179 (D)	0.5	NA	NA	NA	NDA	NDA	6/22
	100%	24	2.0	1.0	NDA	NDA	6/23
		48	2.0	2.0	NDA	NDA	6/24
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

① Recording Error
 6/22/81 NDA

Head
 (A)/(B)
 (C)/(D)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 871607

Vehicle Sterile 0.9% Saline

Test

Material Varisoft +75
195-136

Date Animal Received

4/10/81

Source

Dean Dawl

Sex

♂

Date Initiated

6/22/81

Animal No. (Site)	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0160 (A)	0.5	NA	NA	NA	NDV	NDV	6/22
	100%	24	2.0	1.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0160 (B)	0.5	NA	NA	NA	NDV	NDV	6/22
	25%	24	2.0	1.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0160 (C)	0.5	NA	NA	NA	NDV	NDV	6/22
	50%	24	2.0	1.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0160 (D)	0.5	NA	NA	NA	NDV	NDV	6/22
	75%	24	2.0	1.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Head

②/③
②/③

Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8711007

Vehicle Sterile 0.9% Saline

Test Material Varisof + 475
195-136

Date Animal Received 4/10/81

Source Dean Daul Sex ♂

Date Initiated 6/22/81

Animal No. (Site)	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0136 ①	0.5	NA	NA	NA	NDX	NDX	6/22
	75%	24	2.0	2.0	NDX	NDX	6/23
		48	2.0	2.0	NDX	NDX	6/24
0136 ②	0.5	NA	NA	NA	NDX	NDX	6/22
	100%	24	2.0	2.0	NDX	NDX	6/23
		48	2.0	2.0	NDX	NDX	6/24
0136 ③	0.5	NA	NA	NA	NDX	NDX	6/22
	25%	24	1.0	0	NDX	NDX	6/23
		48	2.0	2.0	NDX	NDX	6/24
0136 ④	0.5	NA	NA	NA	NDX	NDX	6/22
	50%	24	2.0	2.0	NDX	NDX	6/23
		48	2.0	2.0	NDX	NDX	6/24
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Head
 (A) / (B)
 (C) / (D)

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8711207

Vehicle Sterile 0.9% Saline

Test

Material

Varisoft +75
195-136

Date Animal Received 4/10/81

Source

Dean Daul

Sex

♂

Date Initiated

6/22/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0189 (A)	0.5	NA	NA	NA	NDV	NDV	6/22
	50%	24	2.0	2.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0189 (B)	0.5	NA	NA	NA	NDV	NDV	6/22
	75%	24	2.0	2.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0189 (C)	0.5	NA	NA	NA	NDV	NDV	6/22
	100%	24	2.0	2.0	NDV	NDV	6/23
		48	2.0	2.0	NDV	NDV	6/24
0189 (D)	0.5	NA	NA	NA	NDV	NDV	6/22
	25%	24	1.0	0	NDV	NDV	6/23
		48	2.0	1.0	NDV	NDV	6/24
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head
 (A) / (B)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No.

8711207

Vehicle

Sterile 0.9% Saline

Test

Material

Varisoft 475
LOT 1138K

Date Animal Received

4/10/81

Source

Deer Paul

Sex

♂

Date Initiated

6/22/81

Animal No. (Site)	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410-							1981
0192 (A)	0.5	NA	NA	NA	NDV	NDV	6/22
	10%	24	1.0	0	NDV	NDV	6/23
		48	1.0	0	NDV	NDV	6/24
0192 (B)	0.5	NA	NA	NA	NDV	NDV	6/22
	10%	24	1.0	0	NDV	NDV	6/23
		48	1.0	0	NDV	NDV	6/24
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable



]

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 7:

**Laboratory Report - Biodegradability
[IQAC 68122-86-1]**

LABORATORY REPORT

Test: Biodegradability

Sample: Varisoft 475

Lab Data:

BOD ₅	53,000	BOD ₂₀	329,000
BOD ₁₀	286,000	BOD ₃₀	416,000

COD (analytical) 2,171,280 mg/L

COD (theoretical) 2,220,000 mg/L

BOD₅/COD 0.02BOD₂₀/COD 0.15BOD₁₀/COD 0.13BOD₃₀/COD 0.19

Reaction Rate Constant 0.07

Results: Based on the above data, we feel Varisoft 475 can be considered biodegradable.

Analytical Procedures:

BOD: In determining the biodegradability of Varisoft 475, our laboratory conducted an Ultimate Oxygen Demand (UOD) study.

The product was aerated for eight (8) weeks with organisms supplied in settled raw sewage to acclimate them to this particular source of food. This was used as our seed material. In the UOD determinations, aliquots were incubated in the presence of the seed material at 20°C. Samples were taken ten (10) consecutive days and also after twenty (20) and thirty (30) days of incubation. BODs were determined on these samples (see attached analyses report), plotted against time and a reaction rate constant calculated.

COD: Chemical Oxygen Demand is determined by refluxing samples in 50% sulfuric acid solution with potassium dichromate which is the oxidizing agent. The amount of $K_2Cr_2O_7$ required to oxidize the sample is the COD.

Carl L. Andrews
Carl Andrews

Director of Laboratory

ANALYSIS REPORT

For Northern Petrochemical Company

2200 East Devon Avenue
Des Plaines, Illinois

Attn: Dr. H. Sanders

Ref No 3157

Date June 11, 1971

[illegible]

Remarks

Results in g/L

Certified by:

Form A141-R1

Unless otherwise noted - results in milligram per liter (mg/L)

186

Carl F. Andrews

Director of Laboratory

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 8:

WARF Institute Reports 8040871 & 8040872 -
Skin Irritation, Eye Irritation, Acute Oral Toxicity
[PEQ 68410-69-5]

WARF INSTITUTE, INC.

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any form of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for Primary Skin Irritation, Primary Eye Irritation,
Acute Oral Toxicity

Description of Sample

Date Received 3-31-78

Reference Number

Sample Code 211-58A
3/31/78

Submitted by Ashland Chemical Company
Janesville, WI

Richard M. Egan

VARISOFT 222-90

Claimed Content

Results Acute Oral LD₅₀: In excess of 5.0 grams per kilogram
of body weight.

✓ Skin irritation index: 5.1

Eye Irritation score:

<u>24 hr</u>	<u>48 hr</u>	<u>72 hr</u>	<u>Day 7</u>
10.8	8.2	6.8	6.7

Method See attached protocols.

Remarks In accordance with FHSA regulations, this product is not toxic orally, is irritating to the skin and is irritating to the eyes.

Signed

by and for the

WARF INSTITUTE, INC.

jb

Date

May 11, 1978

WARF Institute No.

8040871

WARF INSTITUTE, INC.
MADISON, WISCONSIN

ACUTE ORAL TOXICITY

Client: Ashland Chemical Company

WARF Institute No.: 8040871

Sample: Code 211-58A

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: Stomach tubed.

Concentration of Test Material: As submitted.

Results:

<u>Dosage Level [1] (gm/kg)</u>	<u>Average</u> <u>Body Weights (gms)</u>		<u>Mortality</u>	
	<u>Initial</u>	<u>Terminal</u>	<u>Number [2]</u>	<u>Day [3]</u>
5.0	200	303	0/10	-

Oral LD₅₀: In excess of 5.0 grams per kilogram of body weight.

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

* ARS/Sprague Dawley - Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. None of the animals had any remarkable tissue alterations.

WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040871

Sample Code 211-58A

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, 1 abraded area, and 1 intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

Animal Number	24 Hours (1)				72 Hours (1)			
	Abraded		Unabraded		Abraded		Unabraded	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
196	3	2	3	2	3	2	3	2
197	3	2	3	2	3	2	3	2
198	3	2	3	2	3	3	3	3
199	3	2	3	2	3	2	3	2
200	3	2	3	2	3	2	3	2
201	3	2	3	2	3	2	3	2
Score	24-hour		5.0		72-hour		5.2	

Primary Skin Irritation Index (2): 5.1

- (1) Score equals sum of erythema and edema readings.
(2) Skin irritation index equals average of 24 and 72 hour scores.

<u>Erythema and Eschar Formation</u>	<u>Score</u>	<u>Edema Formation</u>	<u>Score</u>
Slight erythema	1	Slight edema (barely perceptible)	1
Defined erythema	2	Defined edema (edges definite rising)	2
Moderate to severe erythema	3	Moderate edema (area raised 1 mm)	3
Severe erythema to slight eschar formation	4	Severe edema (raised more than 1 mm)	4

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client: Ashland Chemical Company

WARF Institute No.: 8040871

Sample: Code 211-58A

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: As submitted.

Special Washing: None

Results:

	Rabbit Number	Cornea		Iris	Conjunctivae		
		Opacity	Area		Redness	Chemosis	Discharge
24 Hour	259	0	0	0	2	0	0
	260	0	0	0	0	0	0
	261	0	0	0	2	1	1
	262	0	0	0	1	0	0
	263	(d) 1	4	1	2	3	3
	264	0	0	0	2	2	1

Eye Irritation Score: 10.8

48 Hour	259	0	0	0	2	0	0
	260	0	0	0	0	0	0
	261	0	0	0	1	0	1
	262	0	0	0	0	0	0
	263	(b) 1	4	1	2	2	3
	264	0	0	0	1	0	0

Eye Irritation Score: 8.2

72 Hour	259	0	0	0	0	0	0
	260	0	0	0	0	0	0
	261	0	0	0	0	0	0
	262	0	0	0	0	0	0
	263	(b) 1	4	1	2	3	3
	264	0	0	0	0	0	0

Eye Irritation Score: 6.8

WARF INSTITUTE, INC.
MADISON, WISCONSIN

EYE IRRITATION (Continued)

Client: Ashland Chemical Company

WARF Institute No.: 8040871

Sample: Code 211-58A

Results:

Rabbit Number	Cornea		Iris	Conjunctivae		
	Opacity	Area		Redness	Chemosis	Discharge
259	0	0	0	0	0	0
260	0	0	0	0	0	0
261	0	0	0	0	0	0
Day 7 262	0	0	0	0	0	0
263 (b)	2	3	0	2	2	1
264	0	0	0	0	0	0

Eye irritation score: 6.7

(b) Sloughing of 25-49% of the corneal epithelium.

(d) Sloughing of 75-100% of the corneal epithelium.

WARF INSTITUTE, INC.

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any form of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for Primary Skin Irritation, Primary Eye Irritation,
Acute Oral Toxicity

Description of Sample Varisoft 222-90X

Date Received 3-31-78

Reference Number

Sample Code 411-58B
3/30/78

Submitted by Ashland Chemical Company
Janesville, WI

Richard M. Egan

Varisoft 222-90

Claimed Content

Results Acute Oral LD₅₀: In excess of 5.0 grams per kilogram
of body weight.

Skin irritation index: 5.2

Eye Irritation score:

<u>24 hr</u>	<u>48 hr</u>	<u>72 hr</u>	<u>Day 7</u>
11.0	3.5	0.8	0.8

Method See attached protocols.

Remarks In accordance with FHSA regulations, this product is not toxic orally, is irritating to the skin and is irritating to the eyes.

Signed *Jean Jensen, Ph.D.*

by and for the WARF INSTITUTE, INC.

jb

Date

May 11, 1978

WARF Institute No.

3040872

WARF INSTITUTE, INC.

MADISON, WISCONSIN

ACUTE ORAL TOXICITY

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: Stomach tubed.

Concentration of Test Material: As submitted.

Results:

<u>Dosage Level [1] (gm/kg)</u>	<u>Average</u> <u>Body Weights (gms)</u>		<u>Mortality</u>	
	<u>Initial</u>	<u>Terminal</u>	<u>Number [2]</u>	<u>Day [3]</u>
5.0	220	310	0/10	-

Oral LD₅₀: In excess of 5.0 grams per kilogram of body weight.

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

* ARS/Sprague Dawley - Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. One of the animals showed atrophy of the right testicle. None of the remaining animals showed any remarkable tissue alterations.

WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, 1 abraded area, and 1 intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: As submitted.

Results:

Animal Number	24 Hours (1)				72 Hours (1)			
	Abraded		Unabraded		Abraded		Unabraded	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
196	3	2	3	2	3	3	3	3
197	3	2	3	2	3	2	3	2
198	3	2	3	2	3	2	3	2
199	3	2	3	2	3	2	3	2
200	3	2	3	2	3	3	3	3
201	3	2	3	2	3	2	3	2

Score 24-hour 5.0

72-hour 5.3

Primary Skin Irritation Index (2): 5.2

- (1) Score equals sum of erythema and edema readings.
(2) Skin irritation index equals average of 24 and 72 hour scores.

<u>Erythema and Eschar Formation</u>	<u>Score</u>	<u>Edema Formation</u>	<u>Score</u>
Slight erythema	1	Slight edema (barely perceptible)	1
Defined erythema	2	Defined edema (edges definite rising)	2
Moderate to severe erythema	3	Moderate edema (area raised 1 mm)	3
Severe erythema to slight eschar formation	4	Severe edema (raised more than 1 mm)	4

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: As submitted

Special Washing: None

Results:

	Rabbit Number	Cornea		Iris	Conjunctivae		
		Opacity	Area		Redness	Chemosis	Discharge
24 Hour	283	1	4	0	2	3	2
	284	0	0	0	2	1	2
	285	0	0	0	0	0	0
	286	0	0	0	2	1	1
	287	0	0	0	1	1	0
	288	0	0	0	2	2	1

Eye Irritation Score: 11.0

48 Hour	283	1	1	0	2	2	1
	284	0	0	0	0	0	0
	285	0	0	0	0	0	0
	286	0	0	0	1	0	0
	287	0	0	0	1	1	0
	288	0	0	0	0	0	0

Eye Irritation Score: 3.5

72 Hour	283	1	1	0	0	0	0
	284	0	0	0	0	0	0
	285	0	0	0	0	0	0
	286	0	0	0	0	0	0
	287	0	0	0	0	0	0
	288	0	0	0	0	0	0

Eye Irritation Score: 0.8

WARF INSTITUTE, INC.
MADISON, WISCONSIN

EYE IRRITATION (Continued)

Client: Ashland Chemical Company

WARF Institute No.: 8040872

Sample: Code 211-58B

Results:

<u>Rabbit</u> <u>Number</u>	<u>Cornea</u>		<u>Iris</u>	<u>Conjunctivae</u>		
	<u>Opacity</u>	<u>Area</u>		<u>Redness</u>	<u>Chemosis</u>	<u>Discharge</u>
283	1	1	0	0	0	0
284	0	0	0	0	0	0
285	0	0	0	0	0	0
Day 7 286	0	0	0	0	0	0
287	0	0	0	0	0	0
288	0	0	0	0	0	0

Eye irritation score: 0.8



]

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 9:

WARF Institute Reports 8040875 & 8040876 -
Skin Irritation, Eye Irritation, Acute Oral Toxicity
[PEQ 68410-69-5, 5% dispersion]

WARF INSTITUTE, INC.

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for Primary Skin Irritation, Primary Eye Irritation, Acute Oral Toxicity

Description of Sample

Date Received 3-31-78

Reference Number 211-58E 3/30/78

Submitted by Ashland Chemical Company
Janesville, WI

Richard M. Egan

5% DISPERSION OF
222-90 LOT 211-58A

Claimed Content

Results

Acute Oral LD₅₀: in excess of 5.0 grams per kilogram of body weight

Skin Irritation Index: 0.8

Eye Irritation Scores:

24 Hr.	48 Hr.	72 Hr.
1.0	Zero	Zero

Method

Please see the attached protocols.

Remarks

In accordance with FHSA regulations, this product is not toxic orally, is not irritating to the skin, and is not irritating to the eyes.

Signed

Jan Jensen, Ph.D.

by and for the WARF INSTITUTE, INC.

Date

May 11, 1978

WARF Institute No. 8040875



WARF INSTITUTE, INC.

MADISON, WISCONSIN

ACUTE ORAL TOXICITY

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: stomach tubed

Concentration of Test Material: as submitted

Results:

<u>Dosage Level [1] (gm/kg)</u>	<u>Average</u> <u>Body Weights (gms)</u>		<u>Mortality</u>	
	<u>Initial</u>	<u>Terminal</u>	<u>Number [2]</u>	<u>Day [3]</u>
5.0	196	279	0/10	

Oral LD₅₀: in excess of 5 gm/kg of body weight

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

* ARS/Sprague Dawley; Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. Two of the animals had lungs that were dark red in color. None of the remaining eight animals showed any remarkable tissue alterations.

WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, 1 abraded area, and 1 intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

Animal Number	24 Hours (1)				72 Hours (1)			
	Abraded		Unabraded		Abraded		Unabraded	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
265	1	0	1	0	0	0	0	0
269	1	0	1	0	1	0	1	0
278	1	1	1	1	0	0	0	0
280	1	1	1	1	0	0	0	0
282	1	0	1	0	0	0	0	0
270	1	0	1	0	0	0	0	0
Score	24-hour		1.3		72-hour		0.2	

Primary Skin Irritation Index (2): 0.8

- (1) Score equals sum of erythema and edema readings.
 (2) Skin irritation index equals average of 24 and 72 hour scores.

<u>Erythema and Eschar Formation</u>	<u>Score</u>	<u>Edema Formation</u>	<u>Score</u>
Slight erythema	1	Slight edema (barely perceptible)	1
Defined erythema	2	Defined edema (edges definite rising)	2
Moderate to severe erythema	3	Moderate edema (area raised 1 mm)	3
Severe erythema to slight eschar formation	4	Severe edema (raised more than 1 mm)	4

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040875

Sample Code 211-58E

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: as submitted

Special Washing: none

Results:

Rabbit Number	Cornea		Iris	Conjunctivae		
	Opacity	Area		Redness	Chemosis	Discharge
24 Hour	13	0	0	0	0	0
	14	0	0	0	0	0
	15	0	0	0	0	0
	16	0	0	0	0	0
	17	0	0	1	0	1
	18	0	0	1	0	0

Eye Irritation Score: 1.0

48 Hour	13	0	0	0	0	0
	14	0	0	0	0	0
	15	0	0	0	0	0
	16	0	0	0	0	0
	17	0	0	0	0	0
	18	0	0	0	0	0

Eye Irritation Score: 0

72 Hour	13	0	0	0	0	0
	14	0	0	0	0	0
	15	0	0	0	0	0
	16	0	0	0	0	0
	17	0	0	0	0	0
	18	0	0	0	0	0

Eye Irritation Score: 0

WARF INSTITUTE, INC.

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for Primary Skin Irritation, Primary Eye Irritation, Acute Oral Toxicity

Description of Sample

Date Received 3-31-78

Reference Number 211-58F

8/30/78

Submitted by Ashland Chemical Company
Janesville, WI

Richard M. Egan

5% DISPERSION
211-58B

Claimed Content

Results

✓ Acute Oral LD₅₀: in excess of 5.0 grams per kilogram of body weight

✓ Skin Irritation Index: 1.0

✓ Eye Irritation Scores:

<u>24 Hr.</u>	<u>48 Hr.</u>	<u>72 Hr.</u>
Zero	Zero	Zero

Method

Please see the attached protocols.

Remarks

In accordance with FHSA regulations, this product is not toxic orally, is not irritating to the skin, and is not irritating to the eyes.

Signed

Jean Jensen P.D.

by and for the WARF INSTITUTE, INC.

Date

May 11, 1978.

WARF Institute No. 8040876

WARF INSTITUTE, INC.
MADISON, WISCONSIN

ACUTE ORAL TOXICITY

Client Ashland Chemical Company

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Male young adult albino rats (approximately 7 weeks of age) of the Sprague Dawley strain* were procured, maintained in group cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Animals were chosen at random from the conditioned animals, dosed as specified and maintained individually in screen bottom cages with continuous access to feed and water for a two week observation period. Observations were made at hourly intervals for 5 hours after dosing and twice daily for the remainder of the two week period. At termination, surviving animals were sacrificed. Gross post mortem examinations were performed on all animals on test and gross tissue alterations noted.

Method of Administration: stomach tubed

Concentration of Test Material: as submitted

Results:

<u>Dosage Level [1] (gm/kg)</u>	<u>Average</u> <u>Body Weights (gms)</u>		<u>Mortality</u>	
	<u>Initial</u>	<u>Terminal</u>	<u>Number [2]</u>	<u>Day [3]</u>
5.0	196	289	0/10	

Oral LD₅₀: in excess of 5 gm/kg of body weight

- [1] Of test material
- [2] Number dead/number dosed
- [3] Period during which deaths were observed

* ARS/Sprague Dawley; Madison, Wisconsin

Other Observations: Necropsies were done on all of the animals. Two of the animals had hemorrhagic content in the small intestine. None of the remaining eight animals showed any remarkable tissue alterations.

WARF INSTITUTE, INC.

MADISON, WISCONSIN

PRIMARY SKIN IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

The hair was clipped from the back and flanks of the animal. The test material was applied to two areas on each rabbit, 1 abraded area, and 1 intact area, in the amount of 0.5 ml per area in the case of liquids or 0.5 gm per area in the case of solids. The treated areas were covered with a gauze patch and taped to maintain the test material in contact with the skin and decrease the rate of evaporation. The animals were immobilized for a 24 hour period at which time the coverings were removed and the degree of erythema and edema were recorded according to the scale below. A second reading was taken at 72 hours. The average of the 24 and 72 hour readings were used to determine the primary irritation index for the sample.

Concentration of Test Material: as submitted

Results:

Animal Number	24 Hours (1)				72 Hours (1)			
	Abraded		Unabraded		Abraded		Unabraded	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
265	1	0	1	0	1	0	1	0
269	1	0	1	0	2	0	2	0
278	1	1	1	0	1	0	0	0
280	1	0	1	0	0	0	0	0
282	1	0	1	0	1	0	1	0
270	1	0	1	0	1	0	1	0
Score	24-hour		1.1		72-hour		0.9	

Primary Skin Irritation Index (2): 1.0

- (1) Score equals sum of erythema and edema readings.
- (2) Skin irritation index equals average of 24 and 72 hour scores.

<u>Erythema and Eschar Formation</u>		Score	<u>Edema Formation</u>		Score
Slight erythema		1	Slight edema (barely perceptible)		1
Defined erythema		2	Defined edema (edges definite rising)		2
Moderate to severe erythema		3	Moderate edema (area raised 1 mm)		3
Severe erythema to slight eschar formation		4	Severe edema (raised more than 1 mm)		4

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client Ashland Chemical Company

WARF Institute No. 8040876

Sample Code 211-58F

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: as submitted

Special Washing: none

Results:

Rabbit Number	Cornea		Iris	Conjunctivae		
	Opacity	Area		Redness	Chemosis	Discharge
24 Hour	19	0	0	0	0	0
	20	0	0	0	0	0
	21	0	0	0	0	0
	22	0	0	0	0	0
	23	0	0	0	0	0
	24	0	0	0	0	0

Eye Irritation Score: 0

48 Hour	19	0	0	0	0	0
	20	0	0	0	0	0
	21	0	0	0	0	0
	22	0	0	0	0	0
	23	0	0	0	0	0
	24	0	0	0	0	0

Eye Irritation Score: 0

72 Hour	19	0	0	0	0	0
	20	0	0	0	0	0
	21	0	0	0	0	0
	22	0	0	0	0	0
	23	0	0	0	0	0
	24	0	0	0	0	0

Eye Irritation Score: 0



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 10:

**Toxicity Studies for Ashland Oil Company
[PEQ 68410-69-5, 4% and 8% dispersions]**

Carisoy 222

AT #10

(4%, 8% solids (H₂O))

Ocular > Irritation
Dermal
Oral LD50

TOXICITY STUDIES

FOR

ASHLAND CHEMICAL COMPANY

COMPILED BY:
Lois Green

REPORTED:
August 7, 1973

REQUESTED BY:
Dr. N.S. Salomons

EYE IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 222 4% Solution Water
Varisoft 222 8% Solution

DRAIZE RABBIT EYE IRRITATION STUDY PROCEDURE

FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

A group of 12 albino rabbits was used in this study to determine the toxicity of the substance _s submitted to eye mucosa. A series of 6 rabbits was used for testing each substance.

One tenth of a milliliter of the product under test was instilled into the conjunctival sacs of the test animals. All treated eyes were unwashed. Ocular evaluations were made with the unaided eye. These evaluations were made at 24, 48 and 72 hours.

The cornea is scored on the basis of the density of the opacity and the total area involved. The iris is scored on the intensity or degree of inflammation exhibited; and the palpebral and bulbar mucosae are scored on the extent of chemosis, hyperemia and discharge.

DRAIZE SCALE FOR SCORING OCULAR LESIONS

1. Cornea
 - A. Opacity-Degree of Density (area which is most dense taken for reading)

Scattered or diffuse area-details of iris clearly visible.....	1
Easily discernible translucent areas, details of iris slightly obscured.....	2
Opalescent areas, no details of iris visible, size of pupil barely discernible.....	3
Opaque, iris invisible.....	4
 - B. Area of Corneal damage involved

One quarter of area (or less) but not zero.....	1
Greater than one quarter, less than one-half.....	2
Greater than one half, less than three quarters.....	3
Greater than three quarters up to whole area.....	4

Score equals A x B x 5 Total maximum - 80
2. Iris
 - A. Values

Folds above normal, congestion, swelling circumcorneal injection (any one or all of these or combination of any thereof), iris still reacting to light, (sluggish reaction is positive).....	1
No reaction to light, hemorrhage; gross destruction (any one or all of these).....	2

Score equals A x 5 Total possible maximum - 10
3. Conjunctivae
 - A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Vessels definitely injected above normal.....	1
More diffuse, deeper crimson red, individual vessels not easily discernible.....	2
Diffuse beefy red.....	3
 - B. Chemosis

Any swelling above normal (includes nictitating membrane).....	1
Obvious swelling with partial eversion of the lids.....	2
Swelling with lids about half closed.....	3
Swelling with lids about half closed to completely closed.....	4
 - C. Discharge

Any amount different from normal (does not include small amount observed in inner canthus of normal animals).....	1
Discharge with moistening of the lids and hairs just adjacent to the lids.....	2
Discharge with moistening of the lids and considerable area around eye.....	3

Score (A + B + C) x 2 Total maximum - 20

The maximum total score is the sum of all scores obtained for the cornea, iris and conjunctivae. Total maximum score possible - 110 points

SCORE SHEET

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
4% Solids

Animal No. 1 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
 4% Solids

Animal No. 2 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
4% Solids

Animal No. 3 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
4% Solids

Animal No. 4 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
 4% Solids

Animal No. 5 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
4% Solids

Animal No. 6 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoit 222
8% Solids

Animal No. 1 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	2	1					
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	4	2					

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
8% Solids

Animal No. 2 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	2	1					
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	4	2					

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
8% Solids

Animal No. 3 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	2	1					
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	4	2					

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
 8% Solids

Animal No. 4 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	1						
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	2						

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
 8% Solids

Animal No. 5 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	2	1					
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	4	2					

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

DRAIZE RABBIT EYE IRRITATION STUDY

Product Tested Varisoft 222
 8% Solids

Animal No. 6 Unwashed

Day	1	2	3	4	5	6	7
Hour	1	Daily Thereafter					
I— CORNEA							
A— Opacity							
B— Area Involved							
II— IRIS							
A— Evaluation							
III— CONJUNCTIVAE							
A— Hyperemia	2	1					
B— Chemosis							
C— Discharge							
Total Points (Total Possible 110)	4	2					

NOTE: ABSENCE OF NUMERICAL SCORING INDICATES SCORES = 0

SUMMARY OF POINTS SCORED

Varisoft 222

4% Solids

8% Solids

PRIMARY IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 222

4% Solids

8% Solids

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN
FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of albino rabbits was used for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

A. Erythema and Eschar Formation	
Very slight erythema (barely perceptible).....	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4
<hr/>	
Total possible erythema score.....	4
<hr/>	
B. Edema Formation	
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm.).....	3
Severe edema (raised more than 1 mm. and extending beyond area of exposure).....	4
<hr/>	
Total possible edema score.....	4
<hr/>	
Total possible score for primary irritation.....	8
or sensitization.....	8
<hr/>	

Primary Irritation Index

2 or less.....mild irritant
2 - 5.....moderate irritant
6 or above.....severe irritant

Sensitization

2 or less.....mild sensitizer
2 - 5.....moderate sensitizer
6 or above.....severe sensitizer

SCORE SHEETS

PRIMARY IRRITATION STUDY

Product Tested Varisoft 222 4% Solids

Test Method ~~Draize~~ Woodard and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBINED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
1	M	0	0	0	0	0.0
2	F	0	0	0	0	
3	F	0	0	0	0	
4	M	0	0	0	0	
5	M	0	0	0	0	
	F	0	0	0	0	
AVERAGE		0.0		0.0		

Primary Irritation Index of Compound 0.0

PRIMARY IRRITATION STUDY

Product Tested Varisoft 222 8% Solids

Test Method Draize Woodward and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBLVED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
-	M	0	0	0	0	0.0
2	F	0	0	0	0	
3	F	0	0	0	0	
	M	0	0	0	0	
5	M	0	0	0	0	
	F	0	0	0	0	
AVERAGE		0.0		0.0		

Primary Irritation Index of Compound 0.0

ACUTE ORAL TOXICITY STUDY

Varisoft 222
4% Solids
8% Solids

METHOD - ACUTE ORAL TOXICITY

A group of approximately 30 albino male and female rats, fasted for twenty-four hours were employed to establish an LD₅₀ range for each product under test.

Young adult rats which had not been used for previous test purposes were assigned to various dose levels at random. Both sexes were equally distributed.

The product under test was placed in a glass syringe and introduced through the esophagus into the stomach with a stainless steel catheter.

Animals on the same dosage level were then placed in a common cage with free access to food and water. The animals were observed daily for a two week period. No postmortem, or histopathology examinations were performed in this particular study.

SCORE SHEETS

ACUTE ORAL TOXICITY ASSAY

Varisoft 222

EXPERIMENTAL DATA

Dosages 0.5 cc./Kg. - 16.0 cc./Kg.

Animals Fasted male & female albino rats

Concentration 4% Solids in aqueous solution

Weights 200-300 grams

Group No.	No. Animals	Dose Level	Number and Day of Deaths														Total	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	S*	D*
I	5	0.5 cc./Kg.															5	0
II	5	1.0 cc./Kg.															5	0
III	5	2.0 cc./Kg.															5	0
IV	5	4.0 cc./Kg.															5	0
V	5	8.0 cc./Kg.															5	0
VI	5	16.0 cc./Kg.															5	0
VII		cc./Kg.																
VIII		cc./Kg.																
IX		cc./Kg.																
X		cc./Kg.																

OBSERVATIONS:

Animals did not exhibit any effects from the test material.

Eating habits and behavior patterns remained normal throughout the observation period.

Equally non-toxic to males & females.

LD₀ = Over 16.0 cc./Kg.

LD₅₀ = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

LD₁₀₀ = Over 16.0 cc./Kg.

* D = Deaths

* S = Survivals

ACUTE ORAL TOXICITY ASSAY

Varisoft 222

EXPERIMENTAL DATA

Dosages 0.5 cc./Kg. - 16.0 cc./Kg. Animals Fasted male & female albino rats
Concentration 8% Solids in aqueous dispersion Weights 200-300 grams

Group No.	No. Animals	Dose Level	Number and Day of Deaths														Total	
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	S*	D*
I	5	0.5 cc./Kg.															5	0
II	5	1.0 cc./Kg.															5	0
III	5	2.0 cc./Kg.															5	0
IV	5	4.0 cc./Kg.															5	0
V	5	8.0 cc./Kg.															5	0
VI	5	16.0 cc./Kg.															5	0
VII		cc./Kg.																
VIII		cc./Kg.																
IX		cc./Kg.																
X		cc./Kg.																

OBSERVATIONS:

Animals did not exhibit any effects from the test material.

Eating habits and behavior patterns remained normal throughout the observation period.

Equally non-toxic to males and females.

LD₀ = Over 16.0 cc./Kg.

LD₅₀ = Over 16.0 cc./Kg. (95% Confidence Limits = Not Established)

LD₁₀₀ = Over 16.0 cc./Kg.

* D = Deaths

* S = Survivals

SUMMARY & CONCLUSIONS

SUMMARY & CONCLUSIONS

OF TOXICITY DATE

SAMPLE Varisoft 222 4% Solids(See Individual Score Sheets
for Detailed Information)**STUDIES PERFORMED**

- X DRAIZE EYE IRRITATION
 X PRIMARY IRRITATION
 X ACUTE ORAL TOXICITY
 ACUTE DERMAL TOXICITY
 DAY SUBACUTE TOXICITY
 ACUTE INHALATION

DRAIZE EYE IRRITATION STUDY				6 albino rabbits		
STRUCTURE	6 eyes unwashed		eyes washed		eyes washed	
	Total Points	Mean Value	Total Points	Mean Value	Total Points	Mean Value
Cornea	0	0.0				
Iris	0	0.0				
Conjunctivae	12	2.0				
Requires labeling under the Federal Hazardous Substances Act.						
X Does not require labeling under the Federal Hazardous Substances Act.						

PRIMARY IRRITATION STUDY		6 albino rabbits
Primary Irritation Index:		
X	Non-primary irritant (score 0.0)	Moderate primary irritant(score2.1-5.0)
	Mild primary irritant (score 0.1-2.0)	Severe primary irritant(score over 6.0)
Requires labeling under the Federal Hazardous Substances Act.		
X	Does not require labeling under the Federal Hazardous Substances Act.	

ACUTE ORAL TOXICITY (single parenteral dose)		X Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats
Acute Oral LD ₅₀ Study:		Federal Hazardous Substances Act Procedure:
<u>LD₅₀ - 95% Confidence</u>		Dosage: 5.0 c.c. or 5.0 gms./Kg.
Over 16.0 cc./Kg. <u>Limits</u>		Deaths:
Not Established		
Requires labeling under the Federal Hazardous Substances Act.		
X Does not require labeling under the Federal Hazardous Substances Act.		

SUMMARY & CONCLUSIONS

OF TOXICITY DATE

SAMPLE Varisoft 222 8%Solids

(See Individual Score Sheets
for Detailed Information)

STUDIES PERFORMED

- X DRAIZE EYE IRRITATION
- X PRIMARY IRRITATION
- X ACUTE ORAL TOXICITY
- ACUTE DERMAL TOXICITY
- DAY SUBACUTE TOXICITY
- ACUTE INHALATION

DRAIZE EYE IRRITATION STUDY 6 albino rabbits						
STRUCTURE	6 eyes unwashed		eyes washed		eyes washed	
	Total Points	Mean Value	Total Points	Mean Value	Total Points	Mean Value
Cornea	0	0.0				
Iris	0	0.0				
Conjunctivae	32	5.3				
Requires labeling under the Federal Hazardous Substances Act.						
X Does not require labeling under the Federal Hazardous Substances Act.						

PRIMARY IRRITATION STUDY 6 albino rabbits	
Primary Irritation Index:	
X Non-primary irritant (score 0.0)	Moderate primary irritant(score 2.1-5.0)
Mild primary irritant (score 0.1-2.0)	Severe primary irritant (score over 6.0)
Requires labeling under the Federal Hazardous Substances Act.	
X Does not require labeling under the Federal Hazardous Substances Act.	

ACUTE ORAL TOXICITY (single parenteral dose)	
X Acute Oral LD ₅₀ Study - 30 albino rats F.H.S.L.A. Procedure - 10 albino rats	
Acute Oral LD ₅₀ Study:	Federal Hazardous Substances Act Procedure:
LD ₅₀ - 95% Confidence Limits	Dosage: 5.0 c.c. or 5.0 gms./Kg.
Over 16.0 cc./Kg. Not Established	Deaths:
Requires labeling under the Federal Hazardous Substances Act.	
X Does not require labeling under the Federal Hazardous Substances Act.	



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 11:

**Report to Ashland Chemical Company - Acute
Toxicity Studies with Varisoft 222
[PEQ 68410-69-5, 4% dispersion]**

Industrial **BIO-TEST** Laboratories, Inc.

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

Oral < D50
Dermal > Irritation
Ocular
4%

REPORT TO

ASHLAND CHEMICAL COMPANY

ACUTE TOXICITY STUDIES WITH
VARISOFT 222

MARCH 15, 1973

IBT NO. 601-02910

✓me

Industrial **BIO-TEST** *Laboratories, Inc.*

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

March 15, 1973

Mr. Robert B. McConnell
Ashland Chemical Company
Division of Ashland Oil, Inc.
Chemical Products Division
2001 Afton Road
Janesville, Wisconsin 53545

Dear Mr. McConnell:

Re: IBT No. 601-02910 - Acute Toxicity
Studies with Varisoft 222

We are submitting herewith our laboratory report dated
March 15, 1973, prepared in connection with the above study.

very truly yours,



J. C. Calandra
President

JCC/kjl

REPORT TO
ASHLAND CHEMICAL COMPANY
ACUTE TOXICITY STUDIES WITH
VARISOFT 222

MARCH 15, 1973

IBT NO. 601-02910

I. Introduction

A sample identified as VARISOFT 222 (4% Solids Dispersion), Lot No. 152-12, was received from Ashland Chemical Company for toxicological evaluation. The following studies were conducted:

Acute Oral Toxicity Study - Albino Rats

Eye Irritation Test - Albino Rabbits

Primary Skin Irritation Test - Albino Rabbits

II. Summary

The results of the acute toxicity studies with VARISOFT 222 (4% Solids Dispersion), Lot No. 152-12, are summarized below.

<u>Test</u>	<u>Results</u>
Acute Oral Toxicity Study - Albino Rats	LD ₅₀ > 34,600 mg/kg
Eye Irritation Test - Albino Rabbits	Minimally Irritating (11.8/110.0)
Primary Skin Irritation Test - Albino Rabbits	Mildly Irritating (1.9/8.0)

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Beverley Kretchmar
Beverley Kretchmar
Technician
Acute Toxicity

Report approved by:

Carmen Mastri
Carmen Mastri, B.S.
Senior Group Leader
Acute Toxicity

M. L. Keplinger
M. L. Keplinger, Ph. D.
Manager, Toxicology

chm

III. Investigational Procedures

A. Acute Oral Toxicity Study - Albino Rats

Young albino rats of the Charles River strain (COBS)* were used as test animals. All animals were kept under observation for five days prior to experimental use, during which period they were checked for general physical health and suitability as test animals. The animals were housed in stock cages and were permitted a standard laboratory diet plus water ad libitum, except during the 16-hour period immediately prior to oral intubation when food was withheld.

Initial screening was conducted in order to determine the general level of toxicity of the test material. Selected groups of four albino rats each (two males and two females) were administered the test material at several dose levels. All doses were administered directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-tipped intubating needle.

After oral administration of the test material, the rats were housed individually in suspended, wire-mesh cages and observed for the following 14 days. Initial and final body weights and reactions were recorded. A necropsy was conducted on all animals sacrificed at the end of the 14-day observation period.

* Charles River Breeding Laboratories, Inc., North Wilmington, Mass.

At the end of the observation period, the acute oral median lethal dose (LD_{50}) of the test material was determined.

B. Eye Irritation Test - Albino Rabbits

Young albino rabbits of the New Zealand strain were used to evaluate the eye irritating properties of the test material. The test method was patterned after that of Draize et al.*.

The test material was instilled into the conjunctival sac of the right eye of each rabbit according to the treatment procedure presented in Table I. The left eye of each animal served as a control. At each scoring interval the cornea, iris, and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system*. The maximum possible score at any one examination and scoring period is 110 points, which indicates maximal irritation and damage to all three ocular tissues. Zero score indicates no irritation. The scoring system is presented in Table II. In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test material. The criteria used for assignment of the descriptive rating are the frequency, the extent, and the persistence of irritation or damage which occur to the three ocular tissues.

* Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

TABLE I
Eye Irritation Test - Albino Rabbits

Treatment Procedure					
Test Material	Number of Animals Evaluated	Form Administered	Quantity of Test Material Administered	Contact Period (seconds)	Volume of Wash (tap water) Scoring Intervals
VARISOFT 222	6	Undiluted	0.1 ml	Unlimited	None One minute, one, 24, and 72 hours, and 7 days

TABLE II

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Grading
Cornea	<u>Opacity (A)</u>	
	Opacity - Degree of density (area which is dense is taken for reading).	
	Scattered or diffuse area, details of iris clearly visible.	1
	Easily discernible translucent areas, details of iris slightly obscured.	2
	Opalescent areas, no details of iris visible, size of pupil barely discernible	3
	Opaque, iris invisible	4
	<u>Area of Cornea Involved (B)</u>	
	One quarter (or less) but not zero	1
	Greater than one-quarter but less than one-half.	2
	Greater than one-half but less than three-quarters.	3
	Greater than three-quarters, up to whole area.	4
	Score equals $A \times B \times 5$ Total maximum = 80	
Iris	<u>Values (A)</u>	
	Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive).	1
	No reaction to light, hemorrhage, gross destruction (any or all of these).	2
	Score equals $A \times 5$ Total maximum = 10	

TABLE II continued

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Grading
Conjunctiva	<u>Redness (A)</u>	
	Redness (refers to palpebral conjunctiva only). Vessels definitely injected above normal.	1
	More diffuse, deeper crimson red, individual vessels not easily discernible.	2
	Diffuse beefy red.	3
	<u>Chemosis (B)</u>	
	Any swelling above normal (includes nictitating membrane).	1
	Obvious swelling with partial eversion of the lids.	2
	Swelling with lids about half-closed.	3
	Swelling with lids about half-closed to completely closed.	4
	<u>Discharge (C)</u>	
	Any amount different from normal (does not in- clude small amount observed in inner canthus of normal animals).	1
	Discharge with moistening of the lids and hairs just adjacent to the lids.	2
	Discharge with moistening of the lids and hairs and considerable area around eye.	3
	Score (A + B + C) x 2	Total maximum = 20

Note: The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctiva.

The rating is arrived at by selecting the maximum mean irritation score at one, 24 or 72 hours after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table III.

TABLE III

Eye Irritation Test - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Non-Irritating	0.0 - 0.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level.
Practically Non-Irritating	> 0.5 - 2.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level.
Minimally Irritating	> 2.5 - 15.0	To maintain this rating, all scores at the 72-hour reading must be zero; otherwise, increase rating one level.
Mildly Irritating	>15.0 - 25.0	To maintain this rating, all scores at the 7-day reading must be zero; otherwise, increase rating one level.
Moderately Irritating	>25.0 - 50.0	To maintain this rating, scores at 7 days must be ≤ 10 for 60% or more of the animals. Also, mean 7-day score must be ≤ 20 . If 7-day mean score is ≤ 20 but $< 60\%$ of animals show scores < 10 , then no animal among those showing scores > 10 can exceed a score of 30 if rating is to be maintained; otherwise, raise rating one level.

TABLE III continued

Eye Irritation Test - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Severely Irritating	>50.0 - 80.0	To maintain this rating, scores at 7 days must be ≤ 30 for 60% or more of the animals. Also, mean 7-day score must be ≤ 40 . If 7-day mean score is ≤ 40 but <60% of the animals show scores ≤ 30 , then no animal among those showing scores > 30 can exceed a score of 60 if rating is to be maintained; otherwise, raise rating one level.
Extremely Irritating	>80.0 - 110.0	

C. Primary Skin Irritation Test - Albino Rabbits

Young albino rabbits of the New Zealand strain were used in the evaluation of the primary skin irritating properties of the test material. The test procedure was modeled after that of Draize et al.*

Prior to the application of the test material, the hair was clipped from the back and flanks of each rabbit. Two test sites located lateral to the midline of the back approximately ten centimeters apart were selected. One of the two sites was abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site remained intact.

Exactly 0.5 ml of undiluted test material (0.5 g of test material moistened with a minimum amount of water in the case of solids) was applied to each of the test sites on each rabbit. The test sites were immediately occluded with two-inch square gauze patches. The patches were placed directly over the test sites and secured with masking tape. The trunk of each animal was then wrapped with impervious plastic sheeting. The wrap held the patches in position and retarded evaporation of the test material during the 24-hour exposure period.

-At the end of 24 hours, the plastic wrappings and patches were removed. The intact and abraded test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. After 72 hours, the sites were reexamined and rescored.

* Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

In evaluating the average irritation present, the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. Similarly, the mean scores for erythema and edema of the abraded test sites after 24 and 72 hours were added. These two values were totaled and divided by four to obtain the mean primary irritation score. The scoring criteria for erythema and edema are shown in Table IV.

The following grading system was used to arrive at a descriptive primary skin irritation rating:

<u>Mean Primary Irritation Score</u> <u>(Range of Values)</u>	<u>Descriptive Rating</u>
0	Non-Irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

TABLE IV

Primary Skin Irritation Test - Albino Rabbits

Scoring Criteria for Skin Reactions

Reaction	Description	Score
Erythema	Barely perceptible (Edges of area not defined)	1
	Pale red in color and area definable	2
	Definite red in color and area well defined	3
	Beet or crimson red in color	4
Edema	Barely perceptible (Edges of area not defined)	1
	Area definable but not raised more than 1 mm	2
	Area well defined and raised approximately 1 mm	3
	Area raised more than 1 mm	4
Injury in Depth	Escharosis, Necrosis	8
Maximum Primary Irritation Score =		8

IV. Results

A. Acute Oral Toxicity Study - Albino Rats

1. Mortality and Body Weights

Individual mortality and body weight data are presented in Table V.

TABLE V
TEST MATERIAL: VARISOFT 222
Acute Oral Toxicity Study - Albino Rats
Mortality and Body Weight Data

Dose* (mg/kg)	Animal Number and Sex	Individual Body Weights (grams)		<u>Number Dead</u> Number Tested	Percent Dead
		Test Day Number:			
		0	14		
10,250	1-M	175	305	0/4	0
	2-M	163	299		
	3-F	161	215		
	4-F	171	221		
15,380	5-M	165	298	0/4	0
	6-M	172	302		
	7-F	158	217		
	8-F	177	224		
23,070	9-M	165	296	0/4	0
	10-M	187	310		
	11-F	168	216		
	12-F	172	229		
34,600	13-M	188	308	0/4	0
	14-M	164	285		
	15-F	153	212		
	16-F	176	224		

Acute Oral LD₅₀ > 34,600 mg/kg

* The test material was administered undiluted.

2. Reactions

The untoward reactions exhibited by the rats following oral administration of VARISOFT 222 included hypoactivity and ruffed fur (all dose levels). Onset of these reactions was noted within one hour after dosing. At the end of 24 hours all animals appeared normal.

Necropsy at sacrifice revealed no gross pathologic alterations among any of the animals.

B. Eye Irritation Test - Albino Rabbits

The results of the eye irritation test are presented in Table VI.

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TABLE VI

TEST MATERIAL: VARISOFT 222

Eye Irritation Test - Albino Rabbits

Results

Tissue	Rabbit Number	1		Hour	24		72	Hours	7
		Minute	Hour		Hours	Days			
Cornea (D-A)	1	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0
Conjunctiva (R-S-D)		8 (2-0-2)	10 (3-1-1), H		0	0	0	0	0
Total		8	10		0	0	0	0	0
Cornea (D-A)	2	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0
Conjunctiva (R-S-D)		8 (1-1-2)	8 (1-1-2)		0	0	0	0	0
Total		8	8		0	0	0	0	0
Cornea (D-A)	3	0	0	0	0	0	0	0	0
Iris		0	5	0	0	0	0	0	0
Conjunctiva (R-S-D)		4 (1-0-1)	12 (2-2-2)		0	0	0	0	0
Total		4	17		0	0	0	0	0
Cornea (D-A)	4	0	0	0	0	0	0	0	0
Iris		0	0	0	0	0	0	0	0
Conjunctiva (R-S-D)		4 (1-0-1)	8 (1-1-2)		0	0	0	0	0
Total		4	8		0	0	0	0	0

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TABLE VI continued

TEST MATERIAL: VARISOFT 222

Eye Irritation Test - Albino Rabbits

Results

Tissue	Rabbit Number	Results				Days
		1 Minute	1 Hour	24 Hours	72 Hours	
Cornea (D-A)	5	0	0	0	0	0
Iris		0	5	0	0	0
Conjunctiva (R-S-D)		8 (1-1-2)	10 (2-1-2)	0	0	0
Total		8	15	0	0	0
Cornea (D-A)	6	0	0	0	0	0
Iris		0	5	0	0	0
Conjunctiva (R-S-D)		4 (1-0-1)	8 (2-1-1)	0	0	0
Total		4	13	0	0	0
Averages						
Cornea		0.0	0.0	0.0	0.0	0.0
Iris		0.0	2.5	0.0	0.0	0.0
Conjunctiva		6.0	9.3	0.0	0.0	0.0
Total		6.0	11.8	0.0	0.0	0.0

H = Hemorrhages

Conjunctiva:

R = Redness

S = Swelling

D = Discharge

Conjunctival Score =
(R+S+D) x 2

Maximum Score = 20

Iris:

Iris Score = Value x 5

Maximum Score = 10

Cornea:

D = Density

A = Area

Corneal Score = D x A x 5

Maximum Score = 80

24
7
168

C. Primary Skin Irritation Test - Albino Rabbits

The results of the primary skin irritation test are presented in Table VII.

TABLE VII

TEST MATERIAL: VARISOFT 222

Primary Skin Irritation Test - Albino Rabbits

Results

Animal Number	Irritation Scores for Abraded Skin Sites At:				Irritation Scores for Intact Skin Sites At:			
	24 Hours		72 Hours		24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
1	2	1	2	0, D	2	0	2	0, D
2	2	1	2	0, D	2	0	2	0, D
3	1	0	1	0	1	0	1	0
4	2	1	2	0, D	2	0	2	0, D
5	2	0	2	0	2	0	2	0
6	2	0	2	0	2	0	2	0
Mean	1.8	0.5	1.8	0.0	1.8	0.0	1.8	0.0
Subtotal	4.1				3.6			

Primary Irritation Score = 1.9

Key:

Er. = Erythema

Ed. = Edema

D = Desquamation



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

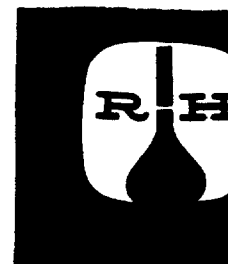
Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 12:

**Rosner-Hixson Laboratories Report - Acute LD50
[PEQ 68410-69-5, 18% dispersion]**

ROSNER-HIXSON LABORATORIES

7737 South Chicago Avenue/Chicago, Illinois 60619/Telephone
Area Code 312 REgent 4-0142



R E P O R T

Laboratory No. PT68-7

Oral LD₅₀ 18% 222

CLIENT: Northern Petrochemical Company of Janesville, Wisconsin.
SAMPLE: Softener 1210 (18% Dispersion of V.222)
OBJECT: To determine the LD₅₀ with special reference to the requirements of the Federal Hazardous Substances Labeling Act.

EXPERIMENTAL AND RESULTS:

Single Oral Doses

The product was diluted 1+1 with 1,2 propanediol employing gentle warming. Ten ml per kg of diluted sample was administered to eight Sprague-Dawley rats previously fasted overnight, and weighing 320 to 395 gm. The oral administration was made by using a syringe with a modified 17 gauge hypodermic needle.

The animals were closely observed following dosing and over a subsequent 14 day observation period, at the conclusion of which they were weighed, sacrificed and subject to a gross autopsy.

All animals survived the 14 day period. On autopsy livers and kidney cortices were darker than usual.

Table 1 gives the initial and final weights of the animals employed

CONCLUSION: The LD₅₀ of Northern Petrochemical Company's Softner 1210 was found to be greater than 5 ml/kg. On this basis the test sample meets the requirements of the Federal Hazardous Substances Labeling Act.

September 9, 1968

ROSNER-HIXSON LABORATORIES

Phillip S. Duke

Phillip S. Duke, Ph.D.
Assistant Technical Director



TABLE 1

ACUTE RAT ORAL TOXICITY

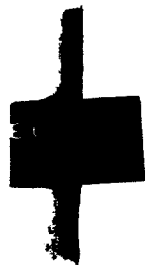
SAMPLE: SOFTENER 1210

SAMPLE ADMINISTERED DILUTED

1 + 1 WITH 1,2 PROPANEDIOL

<u>Animal Number</u>	<u>Body Weight grams</u>	<u>Weight After 14 Days grams</u>	<u>Dose of Diluted Sample ml.</u>	<u>Dosage of Undiluted Sample ml/kg</u>	<u>Days to Death</u>
9	330	363	3.3	5	Survived
10	320	369	3.2	5	Survived
11	320	364	3.2	5	Survived
12	337	378	3.4	5	Survived
13	331	375	3.3	5	Survived
14	395	458	4.0	5	Survived
15	340	392	3.4	5	Survived
16	325	384	3.2	5	Survived

The acute rat oral LD₅₀ of sample was found to be greater than 5 ml/kg



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 13:

WARF Institute Report 7117554 - Primary Eye Irritation
[PEQ 68410-69-5]

WARF INSTITUTE, INC.

MADISON, WISCONSIN

Reports are submitted to clients on a confidential basis. No reference to the work, the results or to the Institute in any of advertising, news release or other public announcement may be made without written authorization from the Institute.

REPORT

Analysis for **Primary Eye Irritation**

Description of Sample **Varisoft 222 - 982**

Date Received **11-16-77**

Reference Number **644750**

Submitted by **Richard M. Egan**
Ashland Chemical Co.
Dublin, OH

Claimed Content

Results

Eye Irritation Scores: $\frac{24 \text{ Hr.}}{14.7}$ $\frac{48 \text{ Hr.}}{8.3}$ $\frac{72 \text{ Hr.}}{4.3}$ $\frac{7 \text{ Day}}{1.0}$ $\frac{14 \text{ Day}}{\text{Zero}}$

Method

Please see the attached protocol.

Remarks

Signed

by and for the

WARF INSTITUTE, INC.

Date

December 21, 1977

WARF Institute No.

7117534

WARF INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION

Client Ashland Chemical Co.

WARF Institute No. 7117554

Sample Varisoft 222 - 90Z 644750

Test Animal: Young adult rabbits (approximately 14 weeks of age) of the New Zealand white strain weighing 2.5 to 3.5 kg were procured, maintained individually in screen bottom cages in air conditioned quarters, provided continuous access to commercial laboratory feed and water and held for a conditioning period of at least 7 days.

Method: Conditioned animals were chosen at random, treated and maintained as specified for the conditioning period.

For each animal treated, one-tenth of a milliliter (0.1 gm for solids) of the test substance was instilled into one eye and the untreated eye served as a control. The reaction to the test material was read according to the scale of scoring for damage at specified times after instillation. Any residue of the test material and accumulated discharge were flushed from the eyes each time they were scored.

Concentration of Test Sample: as submitted

Special Washing: none

Results:

	Rabbit Number	Cornea		Iris	Conjunctivae		
		Opacity	Area		Redness	Chemosis	Discharge
24 Hour	133	1	4	0	2	3	2
	134	0	0	0	2	2	2
	135	0	0	0	2	1	2
	136	0	0	0	2	2	1
	137	0	0	0	2	1	2
	138	0	0	0	2	2	2

Eye Irritation Score: 14.7

48 Hour	133	0	0	0	2	2	2
	134	0	0	0	2	1	1
	135	0	0	0	2	0	0
	136	0	0	0	2	2	1
	137	0	0	0	2	0	1
	138	0	0	0	2	2	1

Eye Irritation Score: 8.3

72 Hour	133	0	0	0	2	1	1
	134	0	0	0	2	0	0
	135	0	0	0	1	0	0
	136	0	0	0	2	1	0
	137	0	0	0	1	0	0
	138	0	0	0	1	1	0

Eye Irritation Score: 4.3

WARE INSTITUTE, INC.

MADISON, WISCONSIN

EYE IRRITATION (CONTINUED)

Client Ashland Chemical Co.

WARE Institute No. 7117554

Sample Varisoft 222 - 90% 644750

Results:

Rabbit Number	Cornea		Iris	Conjunctivae		
	Opacity	Area		Redness	Chemosis	Discharge
133	*DOT	—	—	—	—	—
134	0	0	0	2	1	0
7 Day 135	0	0	0	0	0	0
136	0	0	0	0	0	0
137	0	0	0	0	0	0
138	0	0	0	0	0	0

Eye Irritation Score: 1.0

133	*DOT	—	—	—	—	—
134	*DOT	—	—	—	—	—
14 Day 135	0	0	0	0	0	0
136	0	0	0	0	0	0
137	0	0	0	0	0	0
138	0	0	0	0	0	0

Eye Irritation Score: 0

*The animals that died on test did not appear to be test related.



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

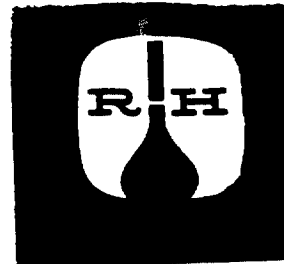
Additional Information and Responses to letter dated
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Attachment 14:

**Rosner-Hixson Laboratories Report - Eye Irritation
[PEQ 68410-69-5, 15% dispersion]**

~~ROSE~~ HIXSON LABORATORIES

Chicago Avenue/Chicago, Illinois 60619/Telephone
Area Code 312 REgent 4-0142



R E P O R T

Laboratory No.

PT71-118

15% 222

Ocular Irritation

CLIENT: Northern Petrochemical Company of Des Plaines, Illinois.

SAMPLE: Varisoft 222, Aqueous Dispersion at 15% Solids Level.

OBJECT: To determine eye irritation potential in accordance with Federal Hazardous Substances Labeling Act Regulations.

EXPERIMENTAL & RESULTS:

The eye irritation properties of sample were tested by instilling 0.1 milliliter into the right eye of each of nine rabbits, the left eye remaining untreated to serve as control.

Rabbits 1-6: eyes unwashed.

Rabbits 7-9: 30 seconds after treatment
eyes washed with 20 milliliters
of water.

Observations of ocular lesions were made on the rabbits' eyes after 24, 48, 72, 96 and 168 hours. At these intervals the extent and degree of irritation were scored. The general technique of evaluation and scoring followed the recommendations of J.H. Draize, G. Woodard and H. O. Calvery, Journal of Pharmacology and Experimental Therapeutics, vol. 82, pg. 377 (1944) and Sec. 191.12 of Federal Hazardous Substances Labeling Act Regulations Guide for Grading Eye Irritation. Fluorescein sodium and ultraviolet light illumination were used to determine extent and degree of irritation. The scores obtained are shown in Table 1.

In rabbits with unwashed eyes, one rabbit showed a grade 1 conjunctival erythema which was normal at 48 hours after treatment. Rabbits with washed eyes showed no eye irritation reaction.

SUMMARY & CONCLUSION:

Varisoft 222, Aqueous Dispersion at 15% Solids Level, was tested for eye irritation in accordance with Federal Hazardous Substances Labeling Act Regulations.

Instillation of sample in eyes of rabbits did not produce a positive eye irritation reaction according to Federal Hazardous Substances Labeling Act Regulations.

On this basis, the sample is not an eye irritant and does not require any precautionary labeling.

May 18, 1971



ROSE-HIXSON LABORATORIES
O. F. Hixson
Technical Director

RABBIT EYE IRRITATION

Rabbit Number	1					2					3				
Hours After Treatment	24	48	72	96	168	24	48	72	96	168	24	48	72	96	168
Cornea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Iris	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Conjunctivae: Erythema	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
Chemosis	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0

[illegible][illegible]



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 15:

**Rosner-Hixson laboratories Report - Skin Irritation
[PEQ 68410-69-5, 4% dispersion]**

6/10/64

Dermal Irritation
70% 222*James*PT64-
PT64-

CLIENT: Varney Chemical Company of Janesville, Wisconsin.

SAMPLE: Two containers labeled Arquad 2HT (4% Dispersion) and Varisoft 222 (4% Dispersion) were received in our laboratory on May 23, 1964.

OBJECT: To determine the skin irritation potential of the subject materials by repeated application to the skin of rabbits.

METHODS: A modification of the technique described by Draize, *et al*⁽¹⁾ was used to study the effects of repeated applications to the products. The hair was clipped from the abdomen of six male albino rabbits, and four areas on the abdomen, approximately ten centimeters apart were designated for application of the products. Two areas on each side of the ventral mid-line were abraded by making four epidermal incisions (two perpendicular to two others in the area of the site) with the point of a 21 gauge needle. The sites were randomized for application of the products to both the intact and abraded sites.

Application of Sample

One-half milliliter of the respective samples was placed on a small square of cotton gauze and maintained in contact with the skin under a larger square of polyethylene film and anchored to the skin with strips of adhesive tape. A square of flannel cloth was then taped around the trunk of the animal to further protect the patches from being dislodged.

After 24 hours the vest and patches were removed and the skin examined for signs of irritation (erythema and/or edema). Examination was made again after 72 hours. The application of the sample was renewed at 72 hours and each subsequent working day for a total of eight applications. Since the patches were not removed on weekends this resulted in a total of twelve days of contact of the products with the skin.

- Continued -

#250-10

June 10, 1964

RESULTS: The initial 24 hour, 72 hour, and 2 week irritation scores are presented in Tables 1 and 2. The primary irritation index for Arquad 2HT, 4% Dispersion, was calculated to be 1.39 and for Varisoft 222, 4% Dispersion, 1.47. Examination of the skin two weeks after the initial application indicated that no significant irritation was present in the case of Arquad 2HT, whereas in the case of Varisoft 222 a minimal degree of erythema and edema was present.

CONCLUSION:

Arquad 2HT and Varisoft 222 when applied as 4% Dispersions repeatedly over a two week period to rabbit skin were found to produce only a minimal degree of skin irritation.

June 10, 1964

ROSNER-HIXSON LABORATORIES

Bob West, Ph.D.
Assistant Director

TABLE 1

SKIN IRRITATION SCORESAROUAD 2HT. 4% DISPERSIONUNABRADED SITES

Rabbit Number	24 Hours		72 Hours		Two Weeks	
	Erythema	Edema	Erythema	Edema	Erythema	Edema
H1410	2	1	0	0	0	0
H1411	1	1	0	0	0	0
H1412	1	1	1	1	0	0
H1413	2	1	0	0	0	0
H1414	2	1	0	0	0	0
H1415	0	0	0	0	0	0
	Average: 2.17		Average: 0.34		Average: 0	

ABRADED SITES

H1410	2	1	0	0	0	0
H1411	1	1	0	0	0	0
H1412	1	1	1	1	0	0
H1413	2	2	0	0	0	0
H1414	2	1	0	0	0	0
H1415	1	1	0	0	0	0
	Average: 2.67		Average: 0.34		Average: 0	

TABLE 2

SKIN IRRITATION SCORESVARISOFT 222. 4% DISPERSIONUNABRADED SITES

Rabbit Number	24 Hours		72 Hours		Two Weeks	
	Erythema	Edema	Erythema	Edema	Erythema	Edema
H1410	1	1	0	0	1	1
H1411	1	1	0	0	2	1
H1412	1	0	0	0	2	1
H1413	2	1	0	0	0	0
H1414	1	1	1	1	0	0
H1415	2	1	0	0	2	1
	Average: 2.17		Average: 0.34		Average: 1.17	

ABRADED SITES

H1410	2	1	1	0	1	1
H1411	1	1	0	0	1	1
H1412	1	1	0	0	1	1
H1413	2	2	0	0	0	0
H1414	1	1	2	1	1	1
H1415	2	1	0	0	2	1
	Average: 2.67		Average: 0.67		Average: 1.83	



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 16:

**Report to Northern Petrochemical Company -
Primary Skin Irritation of Eight Samples of Shampoo
in Albino Rabbits
[PEQ 68410-69-5, Full strength and 4% dispersion]**

*dermal Irritation
test?
8%*

REPORT TO
NORTHERN PETROCHEMICAL COMPANY
PRIMARY SKIN IRRITATION TESTS WITH
EIGHT SAMPLES OF SHAMPOO
IN ALBINO RABBITS

P. O. NO. 54941

MARCH 13, 1972

IBT NO. A1249

I. Introduction

At the request of Northern Petrochemical Company, a primary skin irritation test was conducted with each of eight samples of shampoo. The samples were identified as:

- File —
- ✓ 1. Varisoft 222
 2. 8% Dispersion of Varisoft 222 in water
 3. Varisoft 475
 4. 8% Dispersion of Varisoft 475 in water
 5. Varisoft 100
 6. 8% Dispersion of Varisoft 100 in water
 7. 10% Active Varion CADG in water
 8. 10% Active Tegobetainec in water

II. Summary

The results of the rabbit primary skin irritation tests with eight samples of shampoo are summarized in Table I.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Kenneth Ebbens
Kenneth Ebbens, B.S.
Assistant Toxicologist
Acute Toxicity

Report approved by:

Carmen Mastri
Carmen Mastri, B.S.
Senior Group Leader
Acute Toxicity

M. L. Keplinger
M. L. Keplinger, Ph.D.
Manager, Toxicology

bb

TABLE I
Summary of Results

Test Material	Mean Primary Irritation Score	Results
Varisoft 222	8.0/8.0	Extremely Irritating*
8% Dispersion of Varisoft 222 in water	6.0/8.0	Severely Irritating*
Varisoft 475	8.0/8.0	Extremely Irritating*
8% Dispersion of Varisoft 475 in water	5.1/8.0	Severely Irritating*
Varisoft 100	5.6/8.0	Severely Irritating
8% Dispersion of Varisoft 100 in water	2.8/8.0	Mildly Irritating
10% Active Varion CADG in water	3.3/8.0	Moderately Irritating
10% Active Tegobetainec in water	3.4/8.0	Moderately Irritating

* The chemical burns were superficial and considered not to result in fibrotic tissue replacement.

III. Investigational Procedure

Twelve young albino rabbits of the New Zealand strain were used in the evaluation of the primary skin irritating properties of the test material.

Prior to the application of the test material, the hair was clipped from the back and flanks of each rabbit. Four intact test sites located lateral to the midline of the back approximately ten centimeters apart were selected on each rabbit.

Exactly 0.5 ml of Varisoft 222, 8% Dispersion of Varisoft 222 in water, Varisoft 475 or 8% Dispersion of Varisoft 475 in water was applied to one of the four test sites on six of the rabbits. Varisoft 100, 8% Dispersion of Varisoft 100 in water, 10% Active Varion CADG in water and 10% Active Tegobetainec in water were applied in the same manner to the six remaining rabbits. The test materials were allowed to contact the skin for 24 hours. The sites remained unoccluded during the entire 24-hour contact period.

At the end of the 24-hour contact period the test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. After 72 hours, the sites were reexamined and rescored.

In evaluating the average irritation present for each test material the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. This score was divided by two to obtain the mean primary irritation score. The scoring criteria for erythema and edema are shown in Table II.

The following grading system was used to arrive at a descriptive primary skin irritation rating:

<u>Mean Primary Irritation Score</u> <u>(Range of Values)</u>	<u>Descriptive Rating</u>
0	Non-Irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

TABLE II
Primary Skin Irritation Test - Albino Rabbits
Scoring Criteria for Skin Reactions

Reaction	Description	Score
Erythema	Barely perceptible (Edges of area not defined)	1
	Pale red in color and area definable	2
	Definite red in color and area well defined	3
	Beet or crimson red in color	4
Edema	Barely perceptible (Edges of area not defined)	1
	Area definable but not raised more than 1 mm	2
	Area well defined and raised approximately 1 mm	3
	Area raised more than 1 mm	4
Injury in Depth	Escharosis, Necrosis	8
Maximum Primary Irritation Score =		8

IV. Results -

The results of the primary skin irritation tests are presented in Tables III through X.

TABLE III

TEST MATERIAL: Varisoft 222

Primary Skin Irritation Test - Albino Rabbits

Results - Unoccluded Test Sites

Animal Number	Irritation Scores for Intact Skin Sites at:			
	24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.
1	4	4*	4	4**
2	4	4*	4	4**
3	4	4*	4	4**
4	4	4*	4	4**
5	4	4*	4	4**
6	4	4*	4	4**
Mean	4.0	4.0	4.0	4.0
Subtotal	16.0			
Primary Irritation Score = 8.0				

Key:

Er. = Erythema

Ed. = Edema

* Superficial chemical burns over entire site

** Escharosis

TABLE IV

TEST MATERIAL: 8% Dispersion of Varisoft 222 in water

Primary Skin Irritation Test - Albino Rabbits

Results - Unoccluded Test Sites

Animal Number	Irritation Scores for Intact Skin Sites at:			
	24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.
1	2	1	2	0
2	4	4*	4	4*
3	4	4*	4	4*
4	2	2	2	2
5	3	2	3	2
6	4	4*	4	4*
Mean	3.2	2.8	3.2	2.7
Subtotal	11.9			

Primary Irritation Score = 6.0

Key:

Er. = Erythema

Ed. = Edema

* Superficial chemical burns

1



Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

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Attachment 17:

**Bio-Toxicology Laboratories Report -
DOT and FSHA Skin Irritation
[PEQ 68410-69-5]**

Bio-Toxicology Laboratories, Inc.

Twin Oak Farm Division
Creek & Cox Roads, P. O. Box 267, Moorestown, N. J. 08057
Phone: (609) 665-1776 — 235-2908

January 21, 1974

Normal Irritation
DOT
FSHA

Dr. N.S. Salomons
Ashland Chemical Company
P.O. Box 2219
Columbus, Ohio 43216

Dear Dr. Salomons:

Following are the results of the experimental procedures conducted for Ashland Chemical Company.

MATERIAL:

Varisoft 222 - 90%

Varisoft 110

Varanol SLES-60%

Varanol SLES-30%

Varanol SLS

Varion 1017

RECEIVED:

January 17, 1974

EXPERIMENTAL PERIOD:

January 18 - January 21, 1974

EXPERIMENTAL PROCEDURES:

Primary Irritation Study

The conclusions in this study are based upon the results of the study completed January 21, 1974.

This report is submitted for the exclusive use of Ashland Chemical Company.

Very truly yours,


John Davis Paul
President

JDP/lsd



FDA Registration No. 24-20621

Toxicity and Applied Research Studies - Animal and Human

PRIMARY IRRITATION STUDY

Department of Transportation Act

Varisoft 222-90%

Varisoft 110

Varonol SLES-60%

Varonol SLES-30%

Varonol SLS

Varion 1017

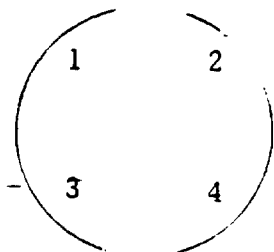
METHOD FOR PRIMARY IRRITATION

DEPARTMENT OF TRANSPORTATION ACT

The intact and abraded skin of 36 albino rabbits was employed for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Four areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. Areas 2 and 3 were abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch). The patches consisted of 1.5 inch x 1.5 inch 12 ply gauze squares. The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml. for liquids and 0.5 gm. for solids) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retard evaporation of volatile substances during the four hour exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis of weighted scores.

Following this initial reading, all test sites were washed with appropriate solvent to prevent further exposure. Readings were again made at 24 and 48 hours after the initial application. Each test substance is evaluated on a total of site (6 abraded and 6 intact).

The primary irritation index is calculated by adding the values for erythema or eschar formation, and edema at 4, 24 and 48 hours on intact and abraded skin (12 values) and dividing by six to obtain an individual score on each rabbit.



2 and 3 = abraded

1 and 4 = intact

1 and 2 = control (if employed)

3 and 4 = test material

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

A. Erythema and Eschar Formation	
Very slight erythema (barely perceptible).....	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4
<hr/>	
Total possible erythema score.....	4
<hr/>	
B. Edema Formation	
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm.).....	3
Severe edema (raised more than 1 mm. and extending beyond area of exposure).....	4
<hr/>	
Total possible edema score.....	4
<hr/>	
Total possible score for primary irritation.....	8
or sensitization.....	8
<hr/>	

Primary Irritation Index

2 or less.....mild irritant
2 - 5.....moderate irritant
6 or above.....severe irritant

Sensitization

2 or less.....mild sensitizer
2 - 5.....moderate sensitizer
6 or above.....severe sensitizer

SCORE SHEETS

Varisoft 222-90%
Varisoft 110
Varonol SLES-60%
Varonol SLES-30%
Varonol SLS
Varion 1017

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 222-90%

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	2	2	2	0	0	0	2.33
	Abraded	2	2	2	0	1	1	
2	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	
3	Intact	2	2	2	0	0	0	2.50
	Abraded	2	2	2	1	1	1	
4	Intact	2	2	2	0	0	0	2.17
	Abraded	2	2	2	0	0	1	
5	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	
6	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	

PRIMARY IRRITATION INDEX OF COMPOUND 2.2

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Product Tested: Varisoft 110

RABBIT #	SKIN	Erythema-eschar observation			Edema observation			AVERAGE
		4 hr.	24 hr.	48 hr.	4 hr.	24 hr.	48 hr.	
1	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	
2	Intact	2	2	1	0	0	0	1.83
	Abraded	2	2	2	0	0	0	
3	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	
4	Intact	2	2	2	0	0	0	2.00
	Abraded	2	2	2	0	0	0	
5	Intact	2	2	1	0	0	0	1.83
	Abraded	2	2	2	0	0	0	
6	Intact	2	2	1	0	0	0	1.83
	Abraded	2	2	2	0	0	0	

PRIMARY IRRITATION INDEX OF COMPOUND

1.9

RATIO OF TISSUE DESTRUCTION:

Test Site	Evaluation of Skin Reaction	Ratio regarding six rabbits Observation time		
		4 hrs.	24 hrs.	48 hrs.
Intact	Non-Corrosive	6:6	6:6	6:6
Abraded	Non-Corrosive	6:6	6:6	6:6

PRIMARY IRRITATION STUDY

Federal Hazardous Substances Labeling Act

Varisoft 222-90%
Varisoft 110
Varonol SLES-60%
Varonol SLES-30%
Varonol SLS
Varion 1017

METHOD FOR PRIMARY IRRITATION-RABBIT SKIN

FEDERAL HAZARDOUS SUBSTANCES LABELING ACT

The intact and abraded skin of 36 albino rabbits was used for this study. A series of 6 rabbits was used for testing each substance. The hair was clipped from the backs with the aid of angora clippers. Two areas of the back, placed approximately ten centimeters apart, were designated for the positions of the patches. One area was abraded by making four epidermal incisions (two perpendicular to two others in the area of the patch.) The patches consisted of two layers of light gauze cut in squares (2.5 cm. on the side). The patches were secured to the area by thin bands of adhesive tape. The material to be tested (0.5 ml.) was introduced beneath the patch. The entire trunks of the animals were then wrapped in clear plastic trunk bands. The trunk bands help to hold the patches in position and retards evaporation of volatile substances during the twenty-four hour exposure. The compound under test was applied so that there were two applications (one intact and one abraded) to each of six animals. The animals were immobilized in a special holder during the twenty-four exposure period. Upon removal of the patches the resulting reactions were evaluated on the basis weighted scores. Evaluations were again made after seventy-two hours. The final score represents an average of the twenty-four and seventy-two hour readings.

METHOD OF POINT SCORING

FOR

EVALUATION OF SKIN REACTIONS

A. Erythema and Eschar Formation	
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth).....	4
<hr/>	
Total possible erythema score	4
<hr/>	
B. Edema Formation	
Very slight edema (barely perceptible).....	1
Slight edema (edges of area well defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm.).....	3
Severe edema (raised more than 1 mm. and extending beyond area of exposure).....	4
<hr/>	
Total possible edema score	4
<hr/>	
Total possible score for primary irritation.....	8
or sensitization	8
<hr/>	

Primary Irritation Index

2 or less.....mild irritant
2 - 5moderate irritant
6 or abovesevere irritant

Sensitization

2 or less.....mild sensitizer
2 - 5moderate sensitizer
6 or abovesevere sensitizer

SCORE SHEETS

Varisoft 222-90%

Varisoft 110

Varonol SLES-60%

Varonol SLES-30%

Varonol SLS

Varion 1017

PRIMARY IRRITATION STUDY

Product Tested Varisoft 222-90%

Test Method Draize Woodard and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBINED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
1	M	2/0	1/0	2/1	2/0	2.08
2	F	2/0	2/0	2/0	2/0	
3	F	2/0	2/0	2/1	2/1	
4	M	2/0	2/0	2/0	2/1	
5	M	2/0	1/0	2/0	2/0	
6	F	2/0	2/0	2/0	2/0	
AVERAGE		1.83		2.33		

Primary Irritation Index of Compound 2.08

Erythema/Edema

PRIMARY IRRITATION STUDY

Product Tested Varisoft 110

Test Method Draize Woodard and Calvery

ANIMAL NO. SEX		RABBIT SKIN				COMBINED AVERAGE
		INTACT		ABRADED		
		24 HRS.	72 HRS.	24 HRS.	72 HRS.	
1	M	2/0	2/0	2/0	2/0	1.83
2	F	2/0	1/0	2/0	2/0	
3	F	2/0	2/0	2/0	2/0	
4	M	2/0	1/0	2/0	2/0	
5	M	2/0	1/0	2/0	2/0	
6	F	2/0	1/0	2/0	2/0	
AVERAGE		1.67		2.00		

Primary Irritation Index of Compound

Erythema/Edema

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 18:

Report to Ashland Chemical Company - Skin
Sensitization Test with Varisoft 222 in Albino Guinea Pigs
[PEQ 68410-69-5]

Industrial **BIO-TEST** *Laboratories, Inc.*

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

ATT #18

1127

REPORT TO

ASHLAND CHEMICAL COMPANY

SKIN SENSITIZATION TEST WITH
VARISOFT 222
IN ALBINO GUINEA PIGS

APRIL 10, 1973

IBT NO. 601-02910

Industrial **BIO-TEST** *Laboratories, Inc.*

1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

April 10, 1973

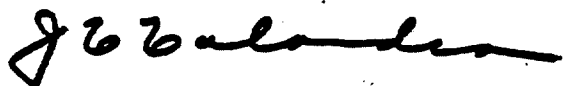
Mr. Robert B. McConnell
Ashland Chemical Company
Division of Ashland Oil, Inc.
Chemical Products Division
2001 Afton Road
Janesville, Wisconsin 53545

Dear Mr. McConnell:

Re: IBT No. 601-02910 - Skin Sensitization Test with
VARISOFT 222 in Albino Guinea Pigs

We are submitting herewith our laboratory report dated
April 10, 1973, prepared in connection with the above study.

Very truly yours,



J. C. Calandra
President

JCC: sjn

REPORT TO
ASHLAND CHEMICAL COMPANY
SKIN SENSITIZATION TEST WITH
VARISOFT 222
IN ALBINO GUINEA PIGS

APRIL 10, 1973

IBT NO. 601-02910

I. Introduction

At the request of Ashland Chemical Company, a skin sensitization test was conducted with a sample identified as VARISOFT 222 (4% Solids Dispersion), Lot No. 152-12.

II. Summary

The results of the skin sensitization test in albino guinea pigs indicate that VARISOFT 222, Lot No. 152-12, is not a sensitizer.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Beverley Kretchmar
Beverley Kretchmar
Technician
Acute Toxicity

Report approved by:

Carmen Mastri
Carmen Mastri, B. S.
Senior Group Leader
Acute Toxicity

M. L. Keplinger
M. L. Keplinger, Ph. D.
Manager, Toxicology

chm

III. Investigational Procedure

Ten albino guinea pigs were used to evaluate the skin sensitizing properties of the test material. The test procedure employed was modeled after that of E. V. Buehler*.

Prior to the test, the irritation threshold of the test material in the appropriate vehicle was established. The hair was then clipped from the backs and flanks of the test animals, and each guinea pig was insulted every other day with a single closed patch containing a non-irritating concentration of the test material for a total of nine insults. Closed patches were applied to the guinea pigs in the following manner: A Webril pad containing 0.5 ml of a 1.0% (w/v) aqueous solution of the test material was applied near the midline of the shaved back of each animal. The Webril pad was occluded with a standard size Elastoplast coverlet (1-1/2 inch x 2 inches) and each animal was placed in a guinea pig restrainer for a six-hour exposure period. The application sites were scored for irritation 24 and 48 hours after the initial insult and 24 hours after each of the remaining eight insults.

Two weeks after the last insult, all test animals and four control animals from the same population were challenged with duplicate patches. The application sites on each animal were scored for irritation 24 and 48 hours after challenge. Any reaction noted among the test animals at challenge that was greater than that noted among the control animals was considered evidence of sensitization.

The scoring criteria for erythema and edema are presented in Table I.

* Buehler, E. V., "Delayed Contact Hypersensitivity in the Guinea Pig," Arch. Dermat. 91, February 1965.

TABLE I
Skin Sensitization Test - Albino Guinea Pigs

Scoring Criteria for Skin Reactions

Reaction	Description	Score
Erythema	Barely perceptible (Edges of area not defined)	1
	Pale red in color and area definable	2
	Definite red in color and area well defined	3
	Beet or crimson red in color	4
Edema	Barely perceptible (Edges of area not defined)	1
	Area definable but not raised more than 1 mm	2
	Area well defined and raised approximately 1 mm	3
	Area raised more than 1 mm	4
Injury in Depth	Escharosis, Necrosis	8
Maximum Primary Skin Irritation Score =		8

IV. Results

The results of the skin sensitization test are presented in Tables
II - IV.

TABLE IV

TEST MATERIAL: 1.0% (w/v) Aqueous Solution of
VARISOFT 222

Skin Sensitization Test - Albino Guinea Pigs

Results - Control Group

Animal Number	Scores Following Challenge Applications							
	Site 1				Site 2			
	24 Hours		48 Hours		24 Hours		48 Hours	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0

Key:

Er. = Erythema

Ed. = Edema

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 19:

**Delayed Contact Hypersensitivity Study in Guinea Pigs
[PEQ 68410-69-5]**

DELAYED CONTACT HYPERSENSITIVITY
STUDY IN GUINEA PIGS

Sample: Varisoft 222-90
Lot V2010225

Lab Study No.: 3063.12
Report Date: 1/18/82

Protocol: Delayed Contact Hypersensitivity

Sponsor: Sherex Company
5200 Blazer Parkway
Dublin, OH 43017

Enclosed:

	<u>Page</u>
Summary	2
GLP Requirements	3
Quality Assurance Statements	4
Raw Data Appendix	5-10
Protocol	11-18
Pertinent Communications	19-23
Protocol Amendment	None

Signed:

Patty Good
Laboratory Technician

Richard A. Hiles
Richard A. Hiles, Ph.D.
Vice President and
Director of Acute and
Subchronic Toxicology
(Study Director)

Jon C. Fulfs
Jon C. Fulfs, Ph.D.
President and Director of
Toxicology

Date 1/18/82

DELAYED CONTACT HYPERSENSITIVITY--SUMMARY

Report of a biological test performed at:

Springborn Institute for Bioresearch, Inc.
553 North Broadway
Spencerville, Ohio 45887

During the period: 11/2/81 to 1/18/82

According to the attached protocol and addenda (if any).

Deviations from Protocol: None

Lab Study No.: 3063.12

Sponsor's Reference: Letter of October 26, 1981

Test Substance (TSIN): Varisoft 222-90 Lot V2010225

Description: Pinkish dull paste

Storage Conditions: Ambient

Sponsor's Divisional Toxicologist: Robert L. Harrison

Strain and Source of Animals: Hartley Albino Guinea Pigs
Isaacs Lab Stock

Concentration and Amount of Test Substance Dosed: Induction: 25% Varisoft 222-90 in 80% Ethanol
Challenge: 2.5% Varisoft w/v in Acetone
Rechallenge: 2.5% Varisoft w/v in distilled H₂O
5.0% Quat A w/v in 95% ETOH¹
0.5% 1208-OS w/v in 95% ETOH²

RESULTS						
Treatment	Level	Incidence	Severity		Max. Score	
			24 hr	48 hr	24 hr	48 hr
Primary Challenge: Test	2.5%	18/19	1.1	0.7	2	1
(Varisoft) Control	2.5%	0/10	0.0	0.1	0	±
Rechallenge: Test	2.5%	0/19	0.1	0.1	±	±
(Varisoft) Control	2.5%	0/6	0.0	0.0	0	0
(Quat A) Test	5%	15/19	1.0	0.6	2	1
Control	5%	1/6	0.5	0.3	1	1
(1208-OS) Test	0.5%	13/19	0.9	0.6	2	1
Control	0.5%	0/6	0.1	0.1	±	±

Conclusions: See page 2(A).

¹From study 3063.11.

²From studies 3063.8, 3063.9, 3063.10.

CONCLUSIONS

Eighteen of nineteen guinea pigs challenged with 2.5% Varisoft 222-90 in acetone exhibited positive (≥ 1 score) responses following three induction exposures with a 25% preparation of Varisoft in ethanol. (The induction exposures caused moderate irritation.) All test animals were rechallenged with 2.5% Varisoft in water and no (0 of 19) animals exhibited positive responses. Thus, the acetone enhances the response to Varisoft probably by changing the absorption of the test article. The test animals were also exposed to 5% Quat A in ethanol and 0.5% 1208-OS in ethanol at the rechallenge with 15 of 19 and 13 of 19 positive responders, respectively. Thus, under certain defined conditions, Varisoft can elicit a sensitization response with cross reactivity to Quat A and 1208-OS. There are conditions under which Varisoft does not elicit a sensitization response.

GLP REPORT REQUIREMENTS

<u>GLP Requirement</u>	<u>Page</u>
Name and Address of Test Facility	2
Date Study Initiated	2
Date Study Completed	2
Objective and Procedures	11
Statistical Methods Used	NA
Test and Control Article Identification	12
Stability of Test and Control Articles	NA
Description of Methods	12
Description of Test System	12
Species, Strain, Substrain, Source of Supply, Age, Sex, Body Weight Range, Number of Animals Used, and Procedure Used for Identification	
Dosage Information	13
Description of Circumstances Which May Have Affected the Data	NA
Name of the Study Director	1
Names of Other Scientists, Professional, and Personnel Involved in this Study	1
Description of Operations Performed on the Data	15
A Summary and Analysis of the Data	2
A Statement of Conclusions Drawn from the Analysis	2
Signed and Dated Reports of Individual Scientists or Other Professionals Involved in the Study	1
Locations Where All Specimens, Raw Data, and Final Report are to be Stored	4
Quality Assurance Statement (signed)	4

NA = Not Applicable

QUALITY ASSURANCE STATEMENT

Study No. 3063.12 Test Substance Varisoft 222-90
Lot V2010225
Type of Study Delayed Contact Hypersensitivity

Listed below are dates that this study was inspected by the Quality Assurance Unit and the dates findings were reported to the Study Director and to Management.

<u>Dates of Inspection</u>	<u>Dates Findings Reported to Study Director</u>	<u>Dates Findings Reported to Management</u>
1-12-82	1-18-82	1-18-82
1-15-82	1-18-82	1-18-82

Location of Raw Data Storage Statement

The original copy of the final report and all raw data will be on file at the testing facility.



Carol S. Davis
Director
Quality Assurance Unit

Date 1-18-82

PRIMARY IRRITATION OBSERVATIONS--SCREENStudy No. 3063.12Test Article Varisoft 222-90

	Animal No. G- -81	Sex	Exposure Level 25%		Exposure Level 15%		Exposure Level 10%		Exposure Level 5%	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 998 -"	F	2	1	1	±	1	1	1	±
2	"- 999 -"	F	2	1	1	±	1	±	±	0
3	"- 1000 -"	F	2	2	1	1	1	1	±	±
4	"- 1001 -"	F	2	1	2	±	2	1	±	±
5	"- -"									
6	"- -"									

Test Article Level: 25% 15% 10% 5%
 Incidence: 4/4 4/4 4/4 1/4
 Severity:
 Sum (24 hr/48 hr) 8.0 / 5.0 5.0 / 2.5 5.0 / 3.5 2.5 / 1.5
 Avg (24 hr/48 hr) 2.0 / 1.3 1.3 / 0.6 1.3 / 0.9 0.6 / 0.4

	Animal No. G- -81	Sex	Exposure Level 2.5%		Exposure Level 1.0%		Exposure Level 0.5%		Exposure Level 0.25%	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 1032 -"	M	±	±	0	0	0	0	0	0
2	"- 1033 -"	M	±	±	0	0	0	0	0	0
3	"- 1034 -"	F	0	0	0	0	0	0	0	0
4	"- 1035 -"	F	±	0	0	0	0	0	0	0
5	"- -"									
6	"- -"									

Test Article Level: 2.5% 1.0% 0.5% 0.25%
 Incidence: 0/4 0/4 0/4 0/4
 Severity:
 Sum (24 hr/48 hr) 1.5 / 1.0 0.0 / 0.0 0.0 / 0.0 0.0 / 0.0
 Avg (24 hr/48 hr) 0.4 / 0.3 0.0 / 0.0 0.0 / 0.0 0.0 / 0.0

(6)

PRIMARY IRRITATION OBSERVATIONS--SCREENStudy No. 3063.12Test Article Varisoft 222-90

	Animal No. G- -81	Sex	Exposure Level 2.5%		Exposure Level 1.0%		Exposure Level		Exposure Level	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 1054 -"	M	Found Dead							
2	"- 1055 -"	M	0	0	0	0				
3	"- 1056 -"	F	0	0	0	0				
4	"- 1057 -"	F	0	0	0	0				
5	"- -"									
6	"- -"									

Test Article Level:

Incidence:

2.5%

0/3

1.0%

0/3

Severity:

Sum (24 hr/48 hr)

0.0 / 0.0

0.0 / 0.0

Avg (24 hr/48 hr)

0.0 / 0.0

0.0 / 0.0

	Animal No. G- -81	Sex	Exposure Level		Exposure Level		Exposure Level		Exposure Level	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- -"									
2	"- -"									
3	"- -"									
4	"- -"									
5	"- -"									
6	"- -"									

Test Article Level:

Incidence:

Severity:

Sum (24 hr/48 hr)

Avg (24 hr/48 hr)

ADDENDUM TO FINAL REPORT

(7)

OBSERVATIONS--TEST

Study No. 3063.12 Test Article 222-90 Varisoft Phase Challenge

Last induction 12/3/81, Challenge 12/16/81

	Animal No. G- -81	Sex	Exposure Level 2.5%		Exposure Level		Exposure Level		Exposure Level	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 974 -"	M	1	±						
2	"- 975 -"	M	1	±						
3	"- 976 -"	M	1	±*						
4	"- 977 -"	M	1	1						
5	"- 978 -"	M	1	1						
6	"- 979 -"	M	1	±*						
7	"- 980 -"	M	1	±						
8	"- 981 -"	M	1	±*						
9	"- 982 -"	M	Dead							
10	"- 983 -"	M	1	1*						
11	"- 984 -"	F	2	1*						
12	"- 985 -"	F	1	±*						
13	"- 986 -"	F	2	1*						
14	"- 987 -"	F	0	0*						
15	"- 988 -"	F	1	±*						
16	"- 989 -"	F	1	±						
17	"- 990 -"	F	1	1						
18	"- 991 -"	F	1	±						
19	"- 992 -"	F	1	±*						
20	"- 993 -"	F	1	1						

Test Article Level: 2.5%

Incidence: 18/19

Severity:

Sum (24 hr/48 hr) 20.0/12.5

Avg (24 hr/48 hr) 1.1/ 0.7

*See page (7A).

During the grading at 24 hours, I noticed that around the test site there seemed to be an interaction between the tape of the patch and the skin. This was in some control and some test animals. This skin was a little redder than the patch area particularly in the controls. The technician noted that the tape had stuck rather firmly to some animals. We did not systematically record this observation at the 24 hour reading.

At the 48 hour reading, we noted the involved animals with an asterick. In the test animals the tape area was often redder than the test site by one grade. However, in the control and in the test animals more often than not the hair had not grown back in the involved tape area. There was no sign of irritation in the tape area of the involved control animal but rather no hair growth.

ADDENDUM TO FINAL REPORT

(8)

OBSERVATIONS--CONTROL

Study No. 3063.12 Test Article Varisoft. 222-90 Phase Challenge

Challenge 12/16/81

	Animal No. G- -81	Sex	Exposure Level 2.5%		Exposure Level		Exposure Level		Exposure Level	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 1079-"	M	0	0						
2	"- 1080-"	M	0	±						
3	"- 1081-"	M	0	0*						
4	"- 1082-"	M	0	0*						
5	"- 1083-"	M	0	0*						
6	"- 1084-"	F	0	0						
7	"- 1085-"	F	0	0*						
8	"- 1086-"	F	0	0*						
9	"- 1087-"	F	0	0*						
10	"- 1088-"	F	0	0*						

Test Article Level: 2.5%

Incidence: 0/10

Severity:

Sum (24 hr/48 hr) 0.0 / 0.5

Avg (24 hr/48 hr) 0.0 / 0.1

*See page (7A).

(9)

OBSERVATIONS--TEST

Study No. 3063.12 Test Article Varisoft, Quat A 1208-0S Phase Rechallenge

	Animal No. G- -81	Sex	Exposure Level 2.5% Varisoft		Exposure Level 5% Quat A		Exposure Level 0.5% 1208-0S		Exposure Level	
			24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1	"- 974 -"	M	0	0	1	±	±	±		
2	"- 975 -"	M	0	0	±	±	1	±		
3	"- 976 -"	M	0	0	1	±	1	±		
4	"- 977 -"	M	±	0	1	±	1	±		
5	"- 978 -"	M	0	0	2	1	2	1		
6	"- 979 -"	M	0	0	1	±	±	±		
7	"- 980 -"	M	±	0	±	±	±	±		
8	"- 981 -"	M	0	0	1	1	1	±		
9	"- 982 -"	M	Dead							
10	"- 983 -"	M	0	0	1	1	1	1		
11	"- 984 -"	F	0	0	1	±	1	±		
12	"- 985 -"	F	0	0	1	±	1	±		
13	"- 986 -"	F	0	0	1	±	1	±		
14	"- 987 -"	F	0	±	1	±	1	±		
15	"- 988 -"	F	0	0	1	1	1	1		
16	"- 989 -"	F	0	0	1	±	±	±		
17	"- 990 -"	F	0	0	±	±	±	±		
18	"- 991 -"	F	0	0	2	1	2	1		
19	"- 992 -"	- F	0	0	1	±	±	±		
20	"- 993 -"	F	0	0	0	0	1	1		

Test Article Level: 2.5% Varisoft 5% Quat A 0.5% 1208-0S
Incidence: 0/19 15/19 13/19

Severity:

Sum (24 hr/48 hr) 1.0 / 0.5 18.5/11.5 18.0/12.0 /
Avg (24 hr/48 hr) 0.1 / 0.1 1.0/ 0.6 0.9/ 0.6 /

ADDENDUM TO FINAL REPORT

(10)

OBSERVATIONS--CONTROL

Study No. 3063.12 Test Article Varisoft Quat A 1208-0S Phase Rechallenge

Animal No. G- -81	Sex	Exposure Level 2.5% Varisoft		Exposure Level 5% Quat A		Exposure Level 0.5% 1208-0S		Exposure Level	
		24 hr	48 hr	24 hr	48 hr	24 hr	48 hr	24 hr	48 hr
1 "- 1109-"	M	0	0	±	0	0	0		
2 "- 1110-"	M	0	0	±	±	0	0		
3 "- 1111-"	M	0	0	±	0	0	0		
4 "- 1112-"	F	0	0	±	±	0	0		
5 "- 1113-"	F	0	0	1	1	±	±		
6 "- 1114-"	F	0	0	0	0	0	0		
7 "- "									
8 "- "									
9 "- "									
10 "- "									

Test Article Level:	2.5% Varisoft	5% Quat A	0.5% 1208-0S
Incidence:	<u>0/6</u>	<u>1/6</u>	<u>0/6</u>
Severity:			
Sum (24 hr/48 hr)	<u>0.0 / 0.0</u>	<u>3.0 / 2.0</u>	<u>0.5 / 0.5</u>
Avg (24 hr/48 hr)	<u>0.0 / 0.0</u>	<u>0.5 / 0.3</u>	<u>0.1 / 0.1</u>

OCT 27 1981 10 11

SPRINGBORN INSTITUTE FOR BIORESEARCH, INC.

DELAYED CONTACT HYPERSENSITIVITY
(Buehler Method - Modified)

3063.12
10 11PURPOSE

To determine if a test article elicits a delayed contact hypersensitivity response in guinea pigs so that it may be compared with more familiar substances.

TEST ARTICLE

All test articles are furnished by the sponsor. They are identified as follows:

Varisoft 222-90 Lot V2010225

S81.019.3063

The sponsor assumes responsibility for any necessary evaluations for purity, strength, stability, etc.

Storage Conditions: Ambient

Known Hazards: Eye irritant, mildly irritating to the skin

SPONSOR

Sherex Company
5200 Blazer Pkwy
Dublin, Ohio 43017

TESTING FACILITY

Springborn Institute for Bioresearch, Inc.
Spencerville, Ohio 45887
(419) 647-4196

PROPOSED STARTING DATE

11/2/81

(completed by SIB)

PROPOSED COMPLETION DATE

1/18/82

(completed by SIB)

(12 weeks from receipt of test article)

Study No. 3063.12

(12)

00006

TEST SYSTEM JUSTIFICATION

The guinea pig is the classical animal for determining delayed contact hypersensitization.

ANIMALS

Albino Guinea Pigs, Isaacs Lab Stock. Equal numbers of males and females is desirable.

20 animals - test animals

10 animals - negative control

4 animals - primary irritation evaluation,
if required

Acclimated \geq 4 days and treat for 4 days during this period for internal parasites. Animals are of a size to fit the restrainers.

ANIMAL IDENTIFICATION

For scientific reasons, individual animals are not identified by ear tag, toe clip, etc. Each cage and restrainer is marked with the animal number. Careful attention is given to see that the proper animal goes into the proper restrainer during treatment and is returned to the proper cage.

HOUSING AND ANIMAL CARE

One/cage during testing in elevated wire mesh cages. 12/12 hour light/dark cycle. Other items according to AAALAC standards.

FOOD AND WATER

Commercial laboratory feed and water freely available at all times.

ADMINISTRATION OF TEST ARTICLE

Irritation Screen:

Exposure of the guinea pigs can be divided into three phases: Irritation, Induction and Challenge.

The Irritation phase has the purpose of determining the proper level of test article to use in the Challenge phase. This proper level should be the highest level which will not cause irritation when applied to the guinea pigs under the conditions which will be used in the Challenge phase. If the test article is known not to be an irritant, the irritation evaluation need not be run. If the irritation potentials are unknown, four levels of test article are normally evaluated using the same

Study No. 3063.12

(13)

solvent which will be used in the "Challenge Phase". If all tested levels cause irritation, additional levels may need to be run. Appendix B is a format for exposure; the position of the different concentrations should be varied to adjust for possible site-to-site variations. The irritation evaluation can be done before or during the induction phase.

___ Do not run an irritation evaluation.

___ Run an irritation evaluation at the following concentration or amounts using Acetone as a solvent:

- | | |
|----|-----------------|
| 1. | <u>25 % w/v</u> |
| 2. | <u>15 %</u> |
| 3. | <u>10 %</u> |
| 4. | <u>5 %</u> |

To be established by
Elvin Newmann (Procter & Gamble)

warm if needed

Remove the hair from the back using a small animal clipper. Do this the day before applying the test article. Apply closed patches to the animals in the following manner (one patch for each level of test article): Apply 0.4 ml of the freshly prepared test article on a 20 X 20 mm Webril pad on a 37 X 40 mm Parke-Davis Readi-Bandage®. Put the animal in the restrainer and apply the patch(es) to the clipped surface as quickly as possible after the substance has been applied to the patch. Occlude the patch with a rubber dental dam pulled taut and fastened to the bottom of the restrainer with clips. Adjust the restrainer to minimize movement of the animal during exposure. Six (6) hours later (5 1/2-6 1/2 hr), remove the dental dam and patch(es), take the animal from the restrainer and place it in its cage.

Approximately 24 hours after initiating the irritation exposure, depilate all animals as described in the "Challenge Phase" and grade the test sites.

Induction Phase:

The purpose of this phase is to dermally expose the animals to test article over a long enough period of time such that if the material is a sensitizer, the animal can develop an immunological response. The level of test article use may be high as to cause excessive systemic toxicity (i.e., death). A level several times greater than the anticipated human exposure should be used if possible. If a solvent other than water is used, it should be different than the solvent which will be used in the "challenge phase."

To be established by Elvin Newmann, Procter & Gamble.

Concentration or level for induction 25% w/v

Solvent 80/20 Ethanol/H₂O - warm if needed

*BINDER clips
Not used Dental Dam
SOLVED GROUND SCREWS
ON RESTRAINERS
PB 1/13/82*

clip the left shoulder of each animal with a small clipper the day before exposure. Apply closed patches to the animals in the test group(s) in the following manner: Apply 0.4 ml of the freshly prepared test substance or solution or a weighed amount of powder on a 20 X 20 mm Webril pad on a 37 X 40 mm Parke-Davis Read-Bandage® (Parke-Davis and Company, Greenwood, South Carolina). Put the animal in the restrainer and apply the patch to the clipped surface as quickly as possible after the substance has been applied to the patch. Occlude the patch with a rubber dental dam pulled taut and fastened to the bottom of the restrainer with binder clips. Adjust the restrainer to minimize movement of the animal during the exposure period. Six (6) hours later, remove the dental dam and patch, take the animal from the restrainer, and place it in its cage. Remove extremely viscous substances by a gentle rinse with warm water before returning the animals to their cages. Repeat the procedure at the same site once a week for the next two (2) weeks for a total of three 6-hour exposures (the interval between induction exposures may vary from 5 to 9 days). After the last induction exposure, leave the animals untreated for approximately two (2) weeks (12-16 days) before primary challenge. Sec 8 pg 1/13/82

Challenge Phase:

The test animals which have had three previous exposures to the test material are again exposed in the challenge phase. In addition, ten animals which have never been exposed to the test article are treated. The level of test article used is the one requested by the sponsor or the one determined in the irritation screen and should be a non-irritating dose. Some organic solvents can elicit a sensitivity response. If a solvent other than water has been used in the induction phase, a different solvent should be used in the challenge phase.

To be established by Elvin Newmann- Procter & Gamble [*Based on Irritation*]
Test article concentration or level _____

Solvent acetone

Challenge the animals previously exposed during the induction period as well as the previously untreated control animals approximately two (2) weeks after the last induction exposure (the time between the last induction exposure and the challenge may vary from 12 to 16 days). Use the same patching procedure as for the "Induction Phase", but apply the patches to a skin site that has not been exposed previously (Appendix A). The site for challenge may be varied if necessary to achieve the objectives of the experiments (e.g., using multiple samples at challenge will require using several sites).

Approximately twenty-four (24) hours after initiating the primary challenge, depilate all animals with Neet Cream or Lotion Hair Remover (Whitehall Laboratories, Inc., New York). Place the depilatory on the test sites and surrounding areas, and leave it on for no more than thirty (30) minutes. Thoroughly wash off the depilatory with a stream of warm, running water, dry the animals with a towel, and return them to their cages.

A minimum of two (2) hour after depilation, grade the test sites on a scale of 0 to 3 (0 - no reaction, \pm = slightly patchy erythema, 1 = slight, but confluent or moderate, patchy erythema, 2 = moderate erythema, 3 = severe erythema with or without edema). Repeat the grading 24 hours later (48 hour grades).

Grades of 1 or greater in the test group indicate sensitization, provided grades of less than 1 are seen on control animals. If grades of 1 or greater are noted on control animals, then the reactions of test animals that exceed the most severe control reaction are presumed to be due to sensitization.

Rechallenge - The sponsor will be notified of animals that are considered sensitized. Verbal instructions for rechallenge will be given by the Sponsor, followed by written confirmation. Animals considered sensitized can be rechallenged 6-10 days after primary challenge, but not before.

REPORT

Report should include date the study was initiated and terminated and the results of both the challenge and any rechallenge in terms of incidence and severity of responses.

- (1) Incidence - The number of animals in each group showing responses of 1 or greater at either 24 or 48 hours divided by the total number of animals tested in that group (e.g., 10/20).
- (2) Severity - The sum of the test grades divided by the total number of animals tested in a given group determined for both 24 and 48 hours (e.g., 0.8 - 0.7). Grades of \pm are equal to 0.5 for calculation of severity indices. All average grades are to be rounded off to the nearest tenth of a unit.

Study No. 3063.12

00014

SPRINGBORN INSTITUTE FOR BIORESEARCH INC

NOTICE

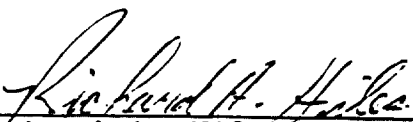
This study is run according to the principles of GLP's. If after a study is underway it becomes necessary to make changes in the approved protocol, the revisions and reasons for change are to be documented, reported to the Sponsor and are to become part of the permanent file for that study. Similarly, the Sponsor is to be notified as soon as is practical whenever an event occurs that is unexpected and may have an effect on the validity of the study.

DATA RETENTION

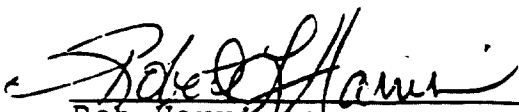
The raw data and the original of the final report will be on file at the testing facility. The sponsor will be notified before final disposition of these items. Unused test articles will be destroyed unless requested otherwise.

REGULATORY AGENCY

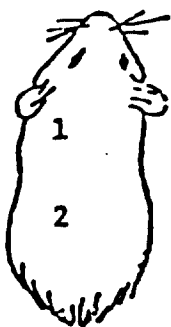
This study will probably not be submitted X, will probably be submitted to a regulatory agency (agency).


Richard A. Hiles, Ph.D.
(SIB) Study Director

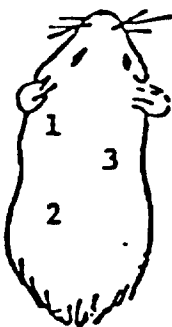
Date 11/2/81


Bob Harrison
Sponsor (Sherex)

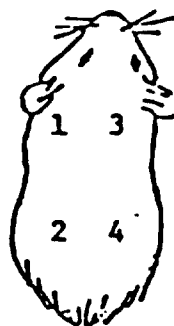
Date 10/26/81

Format for Sensitization Studies1

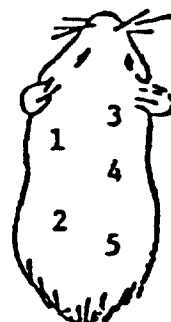
1: Induction
2: Primary Challenge

2

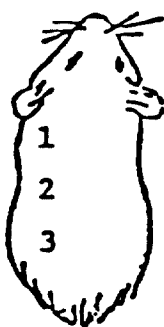
1: Induction
2: Primary Challenge
3: Rechallenge

3

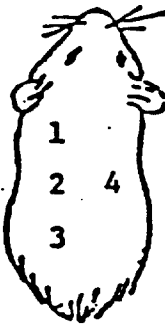
1: Induction
2: Primary Challenge
3,4: Rechallenge

4

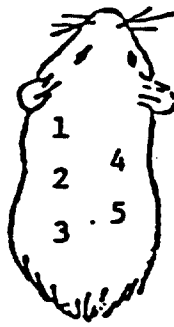
1: Induction
2: Primary Challenge
3-5: Rechallenge

5

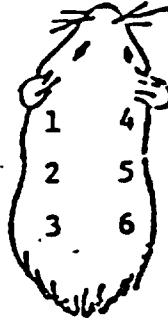
1: Induction
2,3: Primary Challenge

6

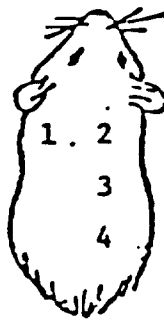
1: Induction
2,3: Primary Challenge
4: Rechallenge

7

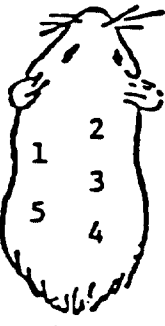
1: Induction
2,3: Primary Challenge
4,5: Rechallenge

8

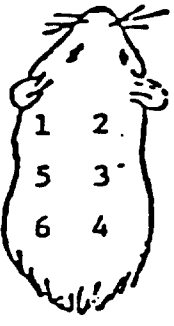
1: Induction
2,3: Primary Challenge
4-6: Rechallenge

9

1: Induction
2-4: Primary Challenge

10

1: Induction
2-4: Primary Challenge
5: Rechallenge

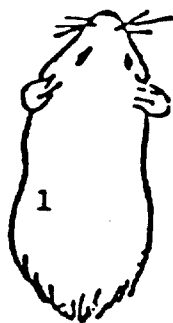
11

1: Induction
2-4: Primary Challenge
5,6: Rechallenge

Appendix B

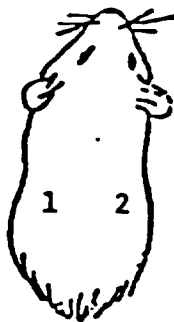
Format for Primary Irritation Study 00020

#1



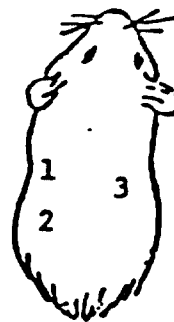
One Test Site

#2



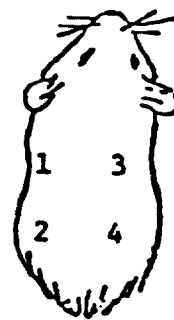
Two Test Sites

#3



Three Test Sites

#4



Four Test Sites

OCT 27 1981

SHEREX

Study No. 3063.12

(19)

SHEREX CHEMICAL COMPANY, INC.

5777 FRANTZ ROAD • P.O. BOX 646

DUBLIN, OHIO 43017

SUBSIDIARY OF SCHERING AG, WEST GERMANY

TEL (614) 764-6500

3063.12
S 81. 019. 3063

October 26, 1981

Dr. Richard Hiles
Springborn Institute for Bioresarch
Spencerville, Ohio 45887

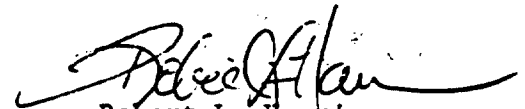
Dear Richard:

You will be receiving under separate cover from Procter & Gamble a sample of Varisoft 222-90 Lot V2010225.

Please initiate a modified Buehler guinea pig sensitization study on this sample according to the attached protocol.

As indicated on the protocol, Elvin Newmann of Procter & Gamble will establish test concentrations, etc.

Very truly yours,


Robert L. Harrison
Manager of Regulatory
Affairs

RLH/dj

Enc.

October 28, 1981

Dr. Richard Hiles
Springborn Institute for Bioresearch Inc.
553 N. Broadway
Spencerville, OH 45887

Dear Dr. Hiles:

Accompanying this note is a sample of Varisoft 222, lot V2-010225 which Sherex Chemical, Inc. (R. L. Harrison) has requested that we send you. Please handle it according to Mr. Harrison's requests. If you have questions, please call Mr. Harrison, Sherex Chemical Company, at 614-764-6559.

Sincerely,

D. J. Kitko

D. J. Kitko

*T.S. received
10/28/81*

Study No. 3063.12
2 December 1981

(21)

SPRINGBORN INSTITUTE FOR BIORESEARCH
SPENCERVILLE OH
PHONE 419 647 419

00036

Dr. R. L. Harrison
Sherex Company
5200 Blazer Parkway
Dublin, OH 43017

Study: 3063.12
Test Article: Varisoft 222-90
Lot V2010225

Confirmation of Telephoned Instructions

Additional Irritation Evaluation using four guinea pigs:

Levels: 2.5% w/v in Acetone
1.0% w/v in Acetone
0.5% w/v in Acetone
0.25% w/v in Acetone

Add \$200.00

Please sign and return one copy.

Sincerely,

SPRINGBORN INSTITUTE FOR
BIORESEARCH, INC.
A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles
Richard A. Hiles, Ph.D.
Vice President and Director
Acute and Subchronic Toxicology

R. L. Harrison
R. L. Harrison

RAH:amb

Date 12/4/81

cc: E. A. Newmann (Procter & Gamble)
- PG
QA



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4 December 1981

SPRINGBORN INSTITUTE FOR BIORESEARCH
SPRINGBORN, OH 43081
PHONE 419 247 4100

Study No. 3063.12

(22)

00038

Dr. R. L. Harrison
Sherex Company
5200 Blazer Parkway
Dublin, OH 43017

Study: 3063.12
Test Article: Varisoft 222.90

Confirmation of Telephoned Instructions

Additional Irritation Evaluation using four guinea pigs:

Levels: 2.5% w/v in Acetone
1.0% w/v in Acetone

Add \$200.00

Please sign and return one copy of this letter.

Sincerely,

SPRINGBORN INSTITUTE FOR
BIORESEARCH, INC.
A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles
Richard A. Hiles, Ph.D.
Vice President and Director
Acute and Subchronic Toxicology

R. L. Harrison

RAH:amb

Date

cc: QA ✓
PG
E. A. Newmann, Procter & Gamble

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processes tested, examined or surveyed and are not necessarily indicative of the qualities of apparently identical or similar materials, products or processes. The liability of Springborn Institute for Bioresearch, Inc. and Springborn Group, Inc. with respect to services rendered is limited to the amount of consideration paid for such services and not include any consequential damages.

JAN 11 1982

(23)

Study No. 3063.12

SPRINGBORN INSTITUTE FOR BIORESEARCH, INC.

SPENCERVILLE, OHIO 43087
PHONE 419 647-4196

4 January 82

Mr. Robert L. Harrison
Sherex Company
5200 Blazer Parkway
Dublin, OH 43017

RE: 3063.12

Dear Mr. Harrison:

As per our telephone conversation of January 4, 1982,
we will rechallenge the guinea pig induced with
Varisoft 222-90 Lot V2010225 as follows:

2.5% w/v Varisoft 222-90 in water.
5% w/v Quat A in 95% ethanol (from 3063.11)
0.5% w/v 1208-05 in 95% ethanol. (from 3063.8, .9, .10)

There will be an additional charge of \$400.00. This charge
includes the extended holding time between the challenge
and the rechallenge.

Please sign and return one copy for our files.

Sincerely,

SPRINGBORN INSTITUTE FOR
BIORESEARCH, INC.
A Member of SPRINGBORN GROUP, INC.

Richard A. Hiles

Richard A. Hiles, Ph.D.
Vice President and Director
Acute and Subchronic Toxicology

Robert L. Harrison
Mr. Robert L. Harrison

Date *1/8/82*

RAH:jl

cc: Accounting
PG
QA-CSD

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Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 20:

Raltech Reports Nos. 816078, 816079, 856938,
856939, 856940, 877521, & 877522 - Skin Sensitization
[PEQ 68410-69-5]



P.O. Box 7545 • Madison, Wisconsin 53707 • 608/241-4471

A Division of Ralston Purina Company

Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

ATT #20

REPORT

S.L. HARRISON
SHEREX CHEMICAL COMPANY, INC.
P.O. BOX 646
DUBLIN, OH 43017

RT LAB NO. 816078

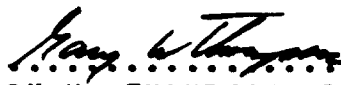
ENTERED 11/13/80

REPORTED 04/02/81

VARISOFT 222-90%: LOT #V2010315

PURCHASE ORDER NUMBER 020-48946 & 53

ENCLOSED: GUINEA PIG SENSITIZATION - METHOD, SUMMARY
RAW DATA ATTACHED

SIGNED: 
GARY W. THOMPSON, ES
HEAD, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.



Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

P.O. Box 7545 • Madison, Wisconsin 53707 • 608/241-4471

A Division of Ralston Purina Company

ST LAB NUMBER 816078

PAGE 2

VARISET 222-90%: LOT #V2010315

SKIN SENSITIZATION

TEST ANIMAL: FOURTEEN MALE ALBINO GUINEA PIGS OF THE HARTLEY STRAIN, WEIGHING BETWEEN 460 AND 514 GRAMS, WERE USED FOR THIS STUDY. THE ANIMAL WERE INDIVIDUALLY HOUSED IN SCREEN BOTTOM CAGES IN A TEMPERATURE AND HUMIDITY CONTROLLED ROOM, PROVIDED CONTINUOUS ACCESS TO COMMERCIAL LABORATORY FEED AND WATER AND HELD FOR AN ACCLIMATION PERIOD OF AT LEAST SEVEN DAYS. EACH ANIMAL WAS IDENTIFIED BY AN ANIMAL NUMBER AND CORRESPONDING EAR TAG. THE ACCLIMATED ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE, UNTREATED CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TEN GUINEA PIGS.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1% WEIGHT TO VOLUME MIXTURE, 1.00 G OF THE TEST MATERIAL WAS WEIGHED INTO AN ERLLENMEYER FLASK. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML.

THE DOSAGE LEVEL WAS SELECTED BASED UPON RESULTS OBTAINED FROM A RANGE FINDING STUDY UTILIZING CONCENTRATIONS OF 1.0%, 10%, 25%, 50%, 75% AND 100% W/V MIXTURES OF TEST MATERIAL IN STERILE 0.9% SALINE.

TREATMENT: PRIOR TO EACH APPLICATION THE HAIR WAS REMOVED FROM THE BACK OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.5 ML OF THE 1% W/V MIXTURE OF TEST MATERIAL ON A WEBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED.

dermal doses

THE TEST GROUP ANIMALS RECEIVED THREE APPLICATIONS PER WEEK FOR THREE WEEKS FOR A TOTAL OF NINE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE NINTH SENSITIZING DOSE, A CHALLENGE DOSE OF 0.5 ML OF A 1% WEIGHT TO VOLUME MIXTURE OF THE TEST MATERIAL IN STERILE 0.9% SALINE WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, A GROUP OF FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WAS ALSO TREATED WITH THIS CHALLENGE DOSE.



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Gray Summit MO

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A Division of Ralston Purina Company

PT LAB NUMBER 816078

PAGE 3

VARISOFT 222-90%: LOT #V2010315

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION ACCORDING TO THE DRA TECHNIQUE.* REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED AT 24 AND 48 HOURS AS WAS DONE FOLLOWING THE SENSITIZING APPLICATIONS. THE ANIMALS WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT WEEKLY INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED.

SENSITIZATION RATINGS

SENSITIZATION RATE

10 - 30%
40 - 70%
80 - 100%

CLASSIFICATION

WEAK SKIN SENSITIZER
MODERATE SKIN SENSITIZER
STRONG SKIN SENSITIZER

*DRAIZE, J.H., 1965, APPRAISAL OF THE SAFETY OF CHEMICALS IN FOODS, DRUGS AND COSMETICS - DERMAL TOXICITY. ASSOCIATION OF FOOD AND DRUG OFFICIALS OF THE U.S., TOPEKA, KANSAS, PP. 49-51.



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RT LAB NUMBER 816078

PAGE 4

VARISOFT 222-90%: LOT #V2010315

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 1/16/81

DATE TEST STARTED: 1/26/81

DATE TEST COMPLETED: 3/1/81

SUMMARY OF SKIN REACTIONS**

TEST GROUP: VARISOFT 222-90% LOT NO. V2010315, 1% W/V
SENSITIZING PHASE
NINE APPLICATIONS
(0.5 ML)

CHALLENGE PHASE
SINGLE APPLICATION
(0.5 ML)

ANIMAL NUMBER	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100001	0.4	(2)	0.3	(2)	0.0	(0)	0.0	(0)
64100002	0.9	(2)	0.6	(2)	0.0	(0)	0.0	(0)
64100003	1.1	(3)	0.7	(2)	0.0	(0)	0.0	(0)
64100004	0.6	(2)	0.1	(1)	0.0	(0)	0.0	(0)
64100005	0.1	(1)	0.0	(0)	0.0	(0)	0.0	(0)
64100006	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100007	0.3	(1)	0.3	(1)	0.0	(0)	0.0	(0)
64100008	0.5	(1)	0.2	(1)	0.0	(0)	0.0	(0)
64100009	0.3	(1)	0.1	(1)	0.0	(0)	0.0	(0)
64100010	0.2	(1)	0.1	(1)	0.0	(0)	0.0	(0)

NAIVE (UNTREATED) CONTROL: (CHALLENGE DOSE - VARISOFT 222-90%
LOT NO. V2010315, 1% W/V)

64100011	-	-	-	-	0.0	(0)	0.0	(0)
64100012	-	-	-	-	0.0	(0)	0.0	(0)
64100013	-	-	-	-	0.0	(0)	0.0	(0)
64100014	-	-	-	-	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE 18 OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.

#V2010315

(CONTINUED)

AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY
THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS
OF ALL ANIMALS DURING THE COURSE OF THE STUDY.

DISCFT 222-90 LOT NO. V2010315, 1% W/V): NINE OF THE
OBSERVED WITH SLIGHT TO MODERATE ERYTHEMA REACTIONS DURING
PHASE OF THE STUDY. SLIGHT TO MODERATE EDEMA REACTIONS
BY EIGHT ANIMALS FOLLOWING THE SENSITIZING APPLICATIONS.
64100006) DID NOT EXHIBIT ANY ERYTHEMA REACTION AND TWO
64100005 AND 64100006) DID NOT EXHIBIT ANY EDEMA REACTIONS
DURING SENSITIZING PHASE OF THE STUDY.

RESULTS IN THE TEST OR NAIVE CONTROL GROUP EXHIBITED EITHER
EDEMA RESPONSE TO THE TEST MATERIAL FOLLOWING THE CHALLENGE
0.5 ML OF A 1.0% W/V MIXTURE OF TEST MATERIAL IN STERILE

TEST MATERIAL IS NOT CONSIDERED A SKIN SENSITIZER IN
THE CLOSED PATCH TECHNIQUE.

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 8110078

Vehicle 19% Saline Test Compound

Varisoft 222



Positive Control Group NA

Vehicle Sterile

LOT NO. V201

(19% w/v)

Animal Number								Tech-nician	Date
6410-0001	6410-0002	6410-0003	6410-0004	6410-0005	6410-0006	6410-0007	6410-0008		
473	477	514	503	488	500	460	477	NA SW	1/26
525	572	562	560	550	538	512	520	CS JP	2/2
584	550	633	651	625	613	578	590	NA	2/9
659	591	687	723	682	668	620	634	SW	2/16
741	643	750	810	768	742	691	705	NA	2/23

		Animal Number		
6410-0009	6410-0010		Tech-nician	Date
				1981
508	510	Scale Used: K-Tron 4809	NDJ SW	1/26
578	562	Scale Used: K-Tron 4809	CS JP	2/2
6210	629	Scale Used: K-Tron 4809	NDJ	2/9
672	681	Scale Used: K-Tron 4809	SW	2/16
743	758	Scale Used: Penn 3728	NDJ	2/23
		Scale Used:		

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Sterile Test Material Varisof 222 LOT NO. V20 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 0410-0001

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NXX	NXX	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NXX	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NXX	NXX	2/5
		48	0	0	SG	SG	2/6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816078

Vehicle 0.9% Saline
Sterile

Test Varisoft 222-9
Material LOT NO. V2010
(1% w/v)

NA

Positive Control Group

NA

Vehicle

NA

6410-
Animal No. 0001

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Daul

Sex

♂

Challenge Date 2/27/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6	0.5	NA	NA	NA	SW	SW	1981 2/16
		24	2.0	1.0	SW	SW	2/17
		48	2.0	2.0	SW	SW	2/18
7	0.5	NA	NA	NA	JP	JP	2/9
		24	2.0	1.0	SW	SW	2/10
		48	1.0	1.0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	1.0	0	JP	JP	2-12
		48	0	0	PP	SW	2/13
9	0.5	NA	NA	NA	JP	JP	2/13
		24	0	0	HN	HN	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1

@recording error at 2-12-81

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Variso .22
Sterile Material LOT NO. V20
(1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0002

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HN	HN	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NJA	NJA	1/28
		24	0	0	HN	HN	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	2.0	1.0	CO	CO	1/31
		48	1.0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	1.0	0	HN	HN	2/3
		48	0	0	NJA	CO	2/4
5	0.5	NA	NA	NA	HN	HN	2/4
		24	0	0	NJA	NJA	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisoft 222-9
Sterile (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0002

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema:	Edema	Technician	Recorded by	Date: 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	2.0	2.0	NA	TP	2/7
		48	2.0	2.0	TP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	2.0 ^D	1.0	NA	SW	2/10
		48	1.0 ^D	1.0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	1.0	1.0	TP	JP	2-12
		48	1.0 ^D	1.0	TP	SW	2/13
9	0.5	NA	NA	NA	TP	TP	2/13
		24	1.0 ^D	1.0	HN	HN	2/14
		48	1.0 ^D	1.0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	TP	TP	2/28
		48	0	0	TP	TP	3/1

^a - Dosage applied by technician indicated

NA - Not Applicable

D = Desquamation SW 2/10/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Varisoft 222-
Sterile Material LOT NO. V201
☐ Positive Control Group NA Vehicle NA Animal No. 0003
6410-
(1% w/v)

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27/

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.5	NA	NA	NA	HH	HH	1981
		24	0	0	SW	SW	1/26
		48	0	0	JP	JP	1/27
2	0.5	NA	NA	NA	NKD	NKD	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NKD	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NKD	NKD	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Sterile Test Material Varisoft 222-9 LOT NO. V2010 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0003

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	2.0	2.0	NDX	TP	2/7
		48	3.0 A	2.0	TP	NDX	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	2.0	2.0	NDX	SW	2/10
		48	2.0 D	2.0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	3.0 DC	2.0	TP	JR	2-12
		48	2.0 D	1.0	TP	SW	2/13
9	0.5	NA	NA	NA	TP	TP	2/13
		24	2.0	1.0	NH	NH	2/14
		48	2.0	1.0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	TP	TP	2/28
		48	0	0	TP	TP	3/1

^a - Dosage applied by technician indicated
 NA - Not Applicable

A = Subcutaneous hemorrhage
2/8/81 N/A

D = Desquamation CO 2/11/81

C = Scale formation JR 2/12/81
① recording another 2/12/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisof 222-9
Sterile (1% w/v) LOT NO. V2010

☐ Positive Control Group NA Vehicle NA Animal No. 10410-
0004

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NXP	NXP	1/28
		24	0	0	HN	HN	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	2.0	1.0	CO	CO	1/31
		48	2.0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	1.0	0	HN	HN	2/3
		48	0	0	NXP	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NXP	NXP	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisoft 222-9
Sterile LOT NO. V2010
(1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 10410-0004

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	NA	TP	2/7
		48	0	0	TP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	1.0	0	TP	JP	2-12
		48	1.0	0	TP	SW	2/13
9	0.5	NA	NA	NA	TP	TP	2/13
		24	1.0	0	NA	NA	2/14
		48	1.0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	TP	TP	2/28
		48	0	0	TP	TP	3/1

^a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Sterile Test Material Varisof 222- LOT NO. V201 (1% wlv)

☐ Positive Control Group NA Vehicle NA Animal No. 0410-0005

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	ND	ND	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	ND	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	ND	ND	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisof 222-9
Sterile (19-wlv) LOT NO. V20103

☐ Positive Control Group NA Vehicle NA Animal No. 10410-0005

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	0	NA	NA	2/7
		48	0	0	NA	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	1.0	0	NA	JR	2-12
		48	0	0	NA	SW	2/13
9	0.5	NA	NA	NA	NA	NA	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	NA	NA	2/28
		48	0	0	NA	NA	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisoft 222
Sterile (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0006

Date Animal Received 1/16/81
 Source Dean Daul Sex ♂

Date Initiated 1/26
 Challenge Date 2/27

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HN	HN	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NJD	NJD	1/28
		24	0	0	HN	HN	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HN	HN	2/3
		48	0	0	NJD	CO	2/4
5	0.5	NA	NA	NA	HN	HN	2/4
		24	0	0	NJD	NJD	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Varisoft 222-9
Sterile Material LOT NO. Y2010
(1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-
0006

Date Animal Received 1/16/81
 Source Dean Daul Sex ♂

Date Initiated 1/26/81
 Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	NA	TP	2/7
		48	0	0	TP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	0	0	TP	JP	2-12
		48	0	0	TP	SW	2/13
9	0.5	NA	NA	NA	TP	TP	2/13
		24	0	0	HH	HH	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	TP	TP	2/28
		48	0	0	TP	TP	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816078

Vehicle 0.9% Saline
Sterile

Test Material Varisoft 222-9
LOT NO. V2010
(1% w/v)



Positive Control Group

NA

Vehicle

NA

10410-
Animal No. 0007

Date Animal Received

1/16/81

Date Initiated

1/26/81

Source

Dean Daul

Sex

♂

Challenge Date

2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	SW	SW	1/28
2	0.5	NA	NA	NA	NOX	NOX	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NOX	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NOX	NOX	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated

NA - Not Applicable

① Recording error HH 2/3/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816078

Vehicle 0.9% Saline
Sterile

Test Varisof 222-9
Material LOT NO. V2010
(1% w/v)



Positive Control Group

NA

Vehicle

NA

6410-
Animal No. 0007

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Daul

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	MP	MP	2/7
		48	- 0	0	MP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	0	NA	SW	2/10
		48	1.0	1.0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2/11
		24	1.0	1.0	MP	JP	2/12
		48	1.0	1.0	MP	SW	2/13
9	0.5	NA	NA	NA	MP	MP	2/13
		24	1.0	1.0	NA	NA	2/14
		48	1.0	1.0	SG	SG	2/15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	MP	MP	2/28
		48	0	0	MP	MP	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Naive
☐ Untreated Control RT No. 816078 Vehicle 0.9% Saline,
Sterile

Date Animal Received 1/16/81

Source Dean Daul Sex ♂

Challenge Date 1/26/81

Animal No.	Dose ^a ml	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6410- 0011	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410- 0012	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410- 0013	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410- 0014	0.5	NA			JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

☐ NA

Test Group RT No. 8110078

Vehicle 0.9% Saline Test Compound

Varisof+222-9

☒

Naive Untreated Control

Sterile

LOT NO. V2010

(1% w/v)

Animal Number								Tech- nician	Date 1981
6410- 0011	6410- 0012	6410- 0013	6410- 0014						
497	489	474	493					NA Sw	1/26
575	573	562	568					CO JP	2/2
666	645	658	648					NA	2/9
719	702	731	707					Sw	2/16
783	786	789	775					NA	2/23
NA	NA	NA	NA					NA	NA

Animal Number								Tech- nician	Date 1981
								NA Sw	1/26
								CO JP	2/2
								NA	2/9
								Sw	2/16
								NA	2/23
								NA	NA

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816078

Vehicle 0.9% Saline
Sterile

Test Material Varisoft 222-9
LOT NO. V2010
(1% w/v)



Positive Control Group

NA

Vehicle

NA

Animal No. 6410-
0010

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Daul

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NOV	NOV	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NOV	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	1.0	0	NOV	NOV	2/5
		48	1.0	0	SG	SG	2/6

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Sterile Test Material Varisoft 222-9 LOT NO. V2010 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0010

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	1.0	NA	NA	2/7
		48	1.0	1.0	NA	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CS	CS	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	0	0	NA	JP	2-12
		48	0	0	NA	SW	2/13
9	0.5	NA	NA	NA	NA	NA	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	NA	NA	2/28
		48	0	0	NA	NA	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

0 = desquamation
2/18/81 NA

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Sterile Test Material Varisoft 222 LOT NO. V201 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0009

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	TH	TH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	SW	SW	1/28
2	0.5	NA	NA	NA	NDA	NDA	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	TH	TH	2/3
		48	0	0	NDA	CO	2/4
5	0.5	NA	NA	NA	TH	TH	2/4
		24	0	0	NDA	NDA	2/5
		48	0	0	SG	SG	2-6

① Recording error JP 1/28b.

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisoft 222
Sterile (1% w/v) LOT NO. V2010

☒ Positive Control Group NA Vehicle NA Animal No. 0009

Date Animal Received 1/16/81

Date Initiated 1/26

Source Dean Daul Sex ♂

Challenge Date 2/27

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	N/A	MP	2/7
		48	0	0	MP	N/A	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	0	N/A	SW	2/10
		48	1.0	0	CD	CD	2/11
8	0.5	NA	NA	NA	SG	SG	2/11
		24	1.0	1.0	MP	JR	2/12
		48	1.0 D	0	MP	SW	2/13
9	0.5	NA	NA	NA	MP	MP	2/13
		24	1.00	0	NH	NH	2/14
		48	1.0 D	0	SG	SG	2/15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	MP	MP	2/28
		48	0	0	MP	MP	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

D = Desquamation SW 2/13/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Varisoft 222-90
Sterile Material LOT NO. V20103
(1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 0008

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	SW	SW	1/27
		48	0	0	JP	JP	1/28
2	0.5	NA	NA	NA	NDX	NDX	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	SW	SW	1/30
		24	0	0	CO	CO	1/31
		48	0	0	CO	CO	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NDX	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	1.0	0	NDX	NDX	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816078 Vehicle 0.9% Saline Test Material Varisoft 222-9
Sterile LOT NO. V2010
(1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0008
 Date Animal Received 1/16/81 Date Initiated 1/26/81
 Source Dean Daul Sex ♂ Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	1.0	NA	NA	2/7
		48	0	0	NA	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	1.0	NA	SW	2/10
		48	1.0	1.0	CO	CO	2/11
8	0.5	NA	NA	NA	SG	SG	2-11
		24	1.0	1.0	NA	JP	2-12
		48	1.0	0	NA	SW	2/13
9	0.5	NA	NA	NA	NA	NA	2/13
		24	1.0	0	NA	NA	2/14
		48	1.0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	NA	NA	2/28
		48	0	0	NA	NA	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable



Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

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A Division of Ralston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90%
(LOT NO. V2010315)

SPONSOR: SHEREX CHEMICAL COMPANY
DUBLIN, OH 43017

STUDY NO. 816078
INITIATION: 1/5/81
COMPLETION: 1/29/81
REPORTED: 2/24/81

SAMPLE: Varisoft 222-90% (Lot No. V2010315)

ENCLOSED: METHOD, PAGE 2 and 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
HEAD, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.



HAZLETON RALTECH, INC.

3301 KINSMAN BLVD. • P O BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 260098 HAZRAL MDS

Guinea Pig Maximization Study
Test Material Varisoft 222-90% (Lot No. V2010315)
Study No. 816078

Sponsor

Sherex Chemical Company
P. O. Box 646
Dublin OH 43017

Contractor

Hazleton Raltech, Inc.
3301 Kinsman Boulevard
Madison WI 53704

Principal Investigator

Robert L. Harrison

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

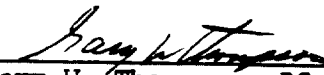
Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of a 5% solution of test material and Freund's Adjuvant Solution."



Gary W. Thompson, BS
Study Director, Acute Toxicology

6-4-82

Date

by and for Hazleton Raltech, Inc.

/dka



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Gray Summit MO

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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010315)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 425 and 494 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010315) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010315) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stirring.

For the topical induction the Varisoft 222-90% (Lot No. V2010315) was administered at a concentration of 25% w/v in sterile saline. For the challenge procedures, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v solution of Varisoft 222-90% (Lot No. V2010315) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and shaving as before. A 1.0% w/v solution of the test material in sterile 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs
Source: Dean Dahl, Luxemburg, Wisconsin
Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010315)

Date Test Started: 1/5/81

Date Test Completed: 1/29/81

<u>Animal Number</u>	<u>Sex</u>	<u>Challenge Dose Reactions</u>	
		<u>24 Hours</u>	<u>48 Hours</u>
64000712	M	0	0
64000713	M	0	0
64000714	M	0	0
64000716	M	0	0
64000717	M	0	0
64000718	M	0	0
64000719	M	0	0
64000721	M	0	0
64000722	M	0	0
64000723	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010315):

None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion: _ _

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010315), is not considered a skin sensitizer.

Reference:

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

Dermal Sensitization In Guinea Pigs - Body Weights

☒ Test Group RT No. 816078 Vehicle NA Test Compound Varisoft 222-9
☐ Positive Control Group NA Vehicle NA LOT NO. V2010315

Animal Number								Tech- nicians	Date
6400-0712	6400-0713	6400-0714	6400-0716	6400-0717	6400-0718	6400-0719	6400-0721		
425	432	472	489	463	449	494	468	NDP	1/12/81
459	485	523	533	501	511	530	517	JP	1/12/81
461	461	542	538	526	515	522	534	JP SW	1/19/81
514	544	627	638	585	558	625	626	JP SW	1/26/81

		Animal Number	Tech- nicians	Date
6400-0722	6400-0723			
493	465	Scale Used: K-Tron 4809	NDP	1/5/81
554	519	Scale Used: K-Tron 4809	JP	1/12/81
548	532	Scale Used: K-Tron 4809	JP SW	1/19/81
662	619	Scale Used: K-Tron 4809	JP SW	1/26/81
		Scale Used:		
		Scale Used:		

NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-9070
 LOT NO. V2010315
 pH Result N/A
 Date Animals Received 12/23/80
 Date of Intradermal Injections 1/5/81
 Date of Topical Application 1/12/81
 Date of Challenge, 1/26/81

RT No. 816078
 Sponsor No. N/A
 Source Dean Dahl
 Technician Co NJP
 Technician Co NJP
 Technician JP

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6400 - 0712 ♂	0		0	
0713 ♂	0		0	
0714 ♂	0		0	
0716 ♂	0		0	
0717 ♂	0		0	
0718 ♂	0		0	
0719 ♂	0		0	
0721 ♂	0		0	
0722 ♂	0		0	
0723 ♂	0		0	
Technician	NH		NH	
Recorded By	NH		NH	
Date	1/28/81		1/29/81	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: NJP DATE: 1/29/81

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 8110078 Vehicle NTD Test Compound Varisof 222-90
 Lot No. 12010315



Positive Control Group VA Vehicle NTD Room No. 1101 B *

Animal Number								Tech- nician	Date 1981
6400- 0712	6400- 0713	6400- 0714	6400- 0716	6400- 0717	6400- 0718	6400- 0719	6400- 0721		
N	N	N	N	N	N	N	N	NDT	1/5/81
N	N	N	N	N	N	N	N	JP	1/6
N	N	N	N	N	N	N	N	JP	1/7
N	N	N	N	N	N	N	N	NDT	1/8
N	N	N	N	N	N	N	N	SG	1-9
N	N	N	N	N	N	N	N	SG	1-10
N	N	N	N	N	N	N	N	SG	1-11
N	N	N	N	N	N	N	N	JP	1/12
N	N	N	N	N	N	N	N	SG	1/13
N	N	N	N	N	N	N	N	SW	1/14
N	N	N	N	N	N	N	N	NDT	1/15
N	N	N	N	N	N	N	N	SW	1/16
N	N	N	N	N	N	N	N	NDT	1/17
N	N	N	N	N	N	N	N	NDT	1/18
N	N	N	N	N	N	N	N	SW	1/19
N	N	N	N	N	N	N	N	JP	1/20
N	N	N	N	N	N	N	N	SG	1-21
N	N	N	N	N	N	N	N	JP	1-22

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 1/15/81 NDT.

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 816078 Vehicle NA Test Compound Varisof 222-90



Positive Control Group NA Vehicle NA Room No. 161 G *
 LOT NO. V201031

Animal Number								Technician	Date
6400-0722	6400-0723								1981
N	N							NA	1/5/81
N	N							JP	1/6
N	N							JP	1/7
N	N							HN	1/8
N	N							SG	1-9
N	N							CG	1/10
N	N							CG	1/11
N	N							JP	1/12
N	N							SG	1/13
N	N							SW	1/14
N	N							HN	1/15
N	N							SW	1/16
N	N							HN	1/17
N	N							HN	1/18
N	N							SW	1/19
N	N							JP	1/20
N	N							SG	1-21
N	N							JP	1-22

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved
 to room 3 on 1/15/81 NA

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 816078 Vehicle NA Test Compound Varisoff 222-90

Positive Control Group NA Vehicle NA Room No. 161 BX

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 1/15/81 NJA

Dermal Sensitization in Guinea Pigs - Daily Observations

Test Group RT No. 816078 Vehicle NA Test Compound Varisoft 222-9

Positive Control Group NA Vehicle NA Room No. 161B * Lot No. V20103

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 1/18/81 NJO



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Guinea Pig Maximization Study
Test Material Varisoft 222-90% (Lot No. V2010315)
Study No. 816078

Sponsor

Sherex Chemical Company
P. O. Box 646
Dublin OH 43017

Contractor

Hazleton Raltech, Inc.
3301 Kinsman Boulevard
Madison WI 53704

Principal Investigator

Robert L. Harrison

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

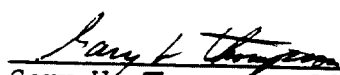
Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of a 5% solution of test material and Freund's Adjuvant Solution."



Gary W. Thompson, BS
Study Director, Acute Toxicology

6-4-82
Date

by and for Hazleton Raltech, Inc.

/dka

RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010315)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 425 and 494 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010315) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010315) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stirring.

For the topical induction the Varisoft 222-90% (Lot No. V2010315) was administered at a concentration of 25% w/v in sterile saline. For the challenge procedures, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v solution of Varisoft 222-90% (Lot No. V2010315) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and shaving as before. A 1.0% w/v solution of the test material in sterile 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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RT LAB NUMBER 816078
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs
Source: Dean Dahl, Luxemburg, Wisconsin
Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010315)

Date Test Started: 1/5/81

Date Test Completed: 1/29/81

<u>Animal Number</u>	<u>Sex</u>	<u>Challenge Dose Reactions</u>	
		<u>24 Hours</u>	<u>48 Hours</u>
64000712	M	0	0
64000713	M	0	0
64000714	M	0	0
64000716	M	0	0
64000717	M	0	0
64000718	M	0	0
64000719	M	0	0
64000721	M	0	0
64000722	M	0	0
64000723	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010315):

None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion: - -

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010315), is not considered a skin sensitizer.

Reference:

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 816078

Vehicle NA

Test Compound Varisof 227-9



Positive Control Group NA

Vehicle NA

LOT NO. VZ010215

Animal Number								Tech- nicians	Date
6400-0712	6400-0713	6400-0714	6400-0716	6400-0717	6400-0718	6400-0719	6400-0721		
425	432	472	489	463	449	494	468	NDV	1/15/81
459	485	523	533	501	511	530	517	JP	1/16/81
461	461	542	538	526	515	522	534	JP	1/17/81
514	544	627	638	585	558	625	626	JP	1/20/81

		Animal Number		Tech- nicians	Date
6400-0722	6400-0723				
493	465	Scale Used: K-Tron 4809		NDV	1/15/81
554	519	Scale Used: K-Tron 4809		JP	1/16/81
548	532	Scale Used: K-Tron 4809		JP	1/19/81
662	619	Scale Used: K-Tron 4809		JP	1/26/81
		Scale Used:			
		Scale Used:			

NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-90%
 LOT NO. V2010315
 pH Result NN
 Date Animals Received 12/23/80
 Date of Intradermal Injections 1/5/81
 Date of Topical Application 1/12/81
 Date of Challenge 1/26/81

RT No. 816078
 Sponsor No. NN
 Source Dean Dahl
 Technician CO NN
 Technician CO NN
 Technician JP

Animal No. - Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6400- 0712 ♂	0		0	
0713 ♂	0		0	
0714 ♂	0		0	
0716 ♂	0		0	
0717 ♂	0		0	
0718 ♂	0		0	
0719 ♂	0		0	
0721 ♂	0		0	
0722 ♂	0		0	
0723 ♂	0		0	
Technician	NN		JP	
Recorded By	NN		JP	
Date	1/28/81		1/29/81	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: NN DATE: 1/29/81

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 8160078 Vehicle NTN Test Compound Varisof 222-90



Positive Control Group NA Vehicle NTN Room No. 161 B *

Animal Number								Tech- nician	Date
6400- 0712	6400- 0713	6400- 0714	6400- 0716	6400- 0717	6400- 0718	6400- 0719	6400- 0721		
N	N	N	N	N	N	N	N	ND	1/5/81
N	N	N	N	N	N	N	N	JP	1/6
N	N	N	N	N	N	N	N	JP	1/7
N	N	N	N	N	N	N	N	ND	1/8
N	N	N	N	N	N	N	N	SG	1/9
N	N	N	N	N	N	N	N	SG	1/10
N	N	N	N	N	N	N	N	SG	1/11
N	N	N	N	N	N	N	N	JP	1/12
N	N	N	N	N	N	N	N	SG	1/13
N	N	N	N	N	N	N	N	SG	1/14
N	N	N	N	N	N	N	N	ND	1/15
N	N	N	N	N	N	N	N	SG	1/16
N	N	N	N	N	N	N	N	ND	1/17
N	N	N	N	N	N	N	N	ND	1/18
N	N	N	N	N	N	N	N	SG	1/19
N	N	N	N	N	N	N	N	JP	1/20
N	N	N	N	N	N	N	N	SG	1-21
N	N	N	N	N	N	N	N	JP	1-22

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 1/15/81 NTN.

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 8110078 Vehicle NA Test Compound Vanisof 222-90



Positive Control Group NA Vehicle NA Room No. 101 B *

LOT NO. V2010315

Animal Number								Tech- nicians	Date
6400- 0722	6400- 0723								1981
N	N							ND	1/5/81
N	N							JP	1/6
N	N							JP	1/7
N	N							ND	1/8
N	N							SG	1/9
N	N							JP	1/10
N	N							JP	1/11
N	N							JP	1/12
N	N							SG	1/13
N	N							SW	1/14
N	N							ND	1/15
N	N							SW	1/16
N	N							ND	1/17
N	N							ND	1/18
N	N							SW	1/19
N	N							JP	1/20
N	N							SG	1-21
N	N							JP	1-22

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved
to room 3 on 1/15/81 ND

Dermal Sensitization in Guinea Pigs - Daily Observations



Positive Control Group: NA Vehicle: NA Room No. 161 BX Lot No. K201051

[illegible]

N - No Visible Abnormalities

NA - Not Applicable.

* Test animals moved to room 3 on 1/15/81 NJP

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 816078 Vehicle NA Test Compound Varisoft 222-9

Positive Control Group NA Vehicle NA Room No. 161B

[illegible]

N - No Visible Abnormalities

NA - Not Applicable.

* Test animals moved to room 3 on 11/19/81 NJO



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ATT #20

REPORT

P.L. HARRISON
SHEREX CHEMICAL COMPANY, INC.
P.O. BOX 646
DUBLIN, OH 43017

RT LAB NO. 816079

ENTERED 11/13/80

REPORTED 04/02/81

VARISOFT 222-907: LOT #V2010225

PURCHASE ORDER NUMBER 020-48946 & 53

ENCLOSED: GUINEA PIG SENSITIZATION - METHOD, SUMMARY
RAW DATA ATTACHED

SIGNED:

Gary W. Thompson
.....
GARY W. THOMPSON, BS
HEAD, ACUTE TOXICOLOGY

BY AND FOR RALTECH SCIENTIFIC SERVICES, INC.



HAZLETON RALTECH, INC.

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Guinea Pig Sensitization (Closed Patch Technique)
Test Material Varisoft 222-90% (Lot No. V20100225)
Study No. 816079

Sponsor

Sherex Chemical Company
P. O. Box 646
Dublin OH 43017

Contractor

Hazleton Raltech, Inc.
3301 Kinsman Boulevard
Madison WI 53704

Principal Investigator

Robert L. Harrison

Study Director

Gary W. Thompson, BS


Amendment No. 1 to the Report

Reason

The "High" score for animal 64100019 is incorrectly listed as (1).

Change

The Challenge Phase erythema high score for animal number 64100019 should be changed to (0).



Gary W. Thompson, BS
Study Director, Acute Toxicology

6-4-82

Date

by and for Hazleton Raltech, Inc.

/dka



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RT LAB NUMBER 816079

PAGE 2

VARISOFT 222-90%: LOT #V2010225

SKIN SENSITIZATION

TEST ANIMAL: FOURTEEN MALE ALBINO GUINEA PIGS OF THE HARTLEY STRAIN, WEIGHING BETWEEN 444 AND 520 GRAMS, WERE USED FOR THIS STUDY. THE ANIMALS WERE INDIVIDUALLY HOUSED IN SCREEN BOTTOM CAGES IN A TEMPERATURE AND HUMIDITY CONTROLLED ROOM, PROVIDED CONTINUOUS ACCESS TO COMMERCIAL LABORATORY FEED AND WATER AND HELD FOR AN ACCLIMATION PERIOD OF AT LEAST SEVEN DAYS. EACH ANIMAL WAS IDENTIFIED BY AN ANIMAL NUMBER AND CORRESPONDING EAP TAG. THE ACCLIMATED ANIMALS WERE DIVIDED INTO TWO GROUPS CONSISTING OF A NAIVE UNTREATED CONTROL GROUP OF FOUR GUINEA PIGS AND A TREATED GROUP OF TEN GUINEA PIGS.

PREPARATION OF TEST MATERIAL: TO PREPARE A 1% WEIGHT TO VOLUME MIXTURE, 1.00 G OF THE TEST MATERIAL WAS WEIGHED INTO AN ERLLENMEYER FLASK. STERILE 0.9% SALINE WAS ADDED TO MAKE A TOTAL VOLUME OF 100 ML.

THE DOSAGE LEVEL WAS SELECTED BASED UPON RESULTS OBTAINED FROM A RANGE FINDING STUDY UTILIZING CONCENTRATIONS OF 1.0, 10.0, 25.0, 50.0, 75.0 AND 100% W/V MIXTURES OF TEST MATERIAL IN STERILE 0.9% SALINE.

TREATMENT: PRIOR TO EACH APPLICATION THE HAIR WAS REMOVED FROM THE BACK OF EACH ANIMAL WITH ELECTRIC CLIPPERS. THE TEST MATERIAL WAS APPLIED TO ONE AREA ON EACH ANIMAL BY PLACING 0.5 ML OF THE 1% W/V MIXTURE OF TEST MATERIAL ON A WEBRIL PAD (7/8 INCH X 1 INCH) AND PLACING THE PAD ON THE TEST SITE ALONG THE MIDLINE OF THE BACK. THE PATCH WAS COVERED WITH RUBBER DAM AND SECURED WITH AN OVERWRAP OF ELASTOPLAST TAPE. THE DRESSING REMAINED IN PLACE FOR A PERIOD OF SIX HOURS AT WHICH TIME IT WAS REMOVED.

THE TEST GROUP ANIMALS RECEIVED THREE APPLICATIONS PER WEEK FOR THREE WEEKS FOR A TOTAL OF NINE APPLICATIONS.

TWO WEEKS FOLLOWING THE ADMINISTRATION OF THE NINTH SENSITIZING DOSE, A CHALLENGE DOSE OF 0.5 ML OF A 1% WEIGHT TO VOLUME MIXTURE OF THE TEST MATERIAL IN STERILE 0.9% SALINE WAS ADMINISTERED TO THE TEST GROUP IN THE SAME MANNER AS DURING THE SENSITIZING PHASE OF THE STUDY. AT THIS TIME, A GROUP OF FOUR NAIVE (PREVIOUSLY UNTREATED) CONTROL ANIMALS WAS ALSO TREATED WITH THE CHALLENGE DOSE.



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PAGE 3

VARISOFT 222-907: LOT #V2010225

SKIN SENSITIZATION (CONTINUED)

OBSERVATIONS: THE APPLICATION SITES WERE READ AND SCORED FOR ERYTHEMA AND EDEMA AT 24 AND 48 HOURS FOLLOWING EACH APPLICATION ACCORDING TO THE DRAIZE TECHNIQUE.* REACTIONS TO THE CHALLENGE DOSE WERE READ AND SCORED AT 24 AND 48 HOURS AS WAS DONE FOLLOWING THE SENSITIZING APPLICATIONS. THE ANIMALS WERE OBSERVED FOR GENERAL BEHAVIOR AND APPEARANCE ONCE DAILY DURING THE ENTIRE STUDY PERIOD. BODY WEIGHTS WERE TAKEN AT STUDY INITIATION AND AT WEEKLY INTERVALS DURING THE STUDY.

PATHOLOGY: AT STUDY TERMINATION ALL ANIMALS WERE EUTHANATIZED AND DISCARDED

SENSITIZATION RATINGS

SENSITIZATION RATE
10 - 30%
40 - 70%
80 - 100%

CLASSIFICATION
WEAK SKIN SENSITIZER
MODERATE SKIN SENSITIZER
STRONG SKIN SENSITIZER

*DRAIZE, J.H., 1965, APPRAISAL OF THE SAFETY OF CHEMICALS IN FOODS, DRUGS AND COSMETICS - DERMAL TOXICITY. ASSOCIATION OF FOOD AND DRUG OFFICIALS OF THE U.S., TOPEKA, KANSAS, PP. 49-51.



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PAGE 4

VARISOFT 222-90%: LOT #V2C10225

SKIN SENSITIZATION (CONTINUED)

TEST ANIMAL: GUINEA PIGS

SOURCE: DEAN DAUL, LUXEMBURG, WI

DATE ANIMALS RECEIVED: 1/16/81

DATE TEST STARTED: 1/26/81

DATE TEST COMPLETED: 3/1/81

SUMMARY OF SKIN REACTIONS**

TEST GROUP: VARISOFT 222-90% LOT NO. V2010225, 1% W/V
SENSITIZING PHASE
NINE APPLICATIONS
(0.5 ML)
CHALLENGE PHASE
SINGLE APPLICATION
(0.5 ML)

ANIMAL NUMBER	ERYTHEMA		EDEMA		ERYTHEMA		EDEMA	
	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)	AVE.	(HIGH)
64100016	0.3	(1)	0.0	(0)	0.0	(0)	0.0	(0)
64100017	0.3	(1)	0.1	(1)	0.0	(0)	0.0	(0)
64100018	0.1	(1)	0.1	(1)	0.0	(0)	0.0	(0)
64100019	0.1	(1)	0.1	(1)	0.0	(1)	0.0	(0)
64100020	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100021	0.5	(1)	0.1	(1)	0.0	(0)	0.0	(0)
64100022	0.1	(1)	0.0	(0)	0.0	(0)	0.0	(0)
64100023	0.0	(0)	0.0	(0)	0.0	(0)	0.0	(0)
64100024	0.6	(2)	0.3	(1)	0.0	(0)	0.0	(0)
64100025	0.6	(2)	0.2	(1)	0.0	(0)	0.0	(0)

NAIVE (UNTREATED) CONTROL: (CHALLENGE DOSE - VARISOFT 222-90%:
LOT NO. V2010225, 1% W/V)

64100026	-	-	-	-	0.0	(0)	0.0	(0)
64100027	-	-	-	-	0.0	(0)	0.0	(0)
64100028	-	-	-	-	0.0	(0)	0.0	(0)
64100029	-	-	-	-	0.0	(0)	0.0	(0)

**THE AVERAGE ERYTHEMA AND EDEMA VALUE IS THE MEAN SCORE FOR THE 18 OBSERVATIONS (SENSITIZING TREATMENT) OR TWO OBSERVATIONS (CHALLENGE TREATMENT) OF THE APPLICATION SITE FOR EACH ANIMAL. THE HIGH READING IS THE HIGHEST SCORE RECORDED FOR THE RESPECTIVE ANIMAL DURING THAT PHASE OF THE STUDY.



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RT LAB NUMBER 816079

PAGE 5

VARISOFT 222-907: LOT #V2010225

SKIN SENSITIZATION (CONTINUED)
RESULTS:

GENERAL BEHAVIOR AND APPEARANCE: ALL OF THE GUINEA PIGS USED IN THIS STUDY APPEARED NORMAL THROUGHOUT THE STUDY PERIOD. NORMAL BODY WEIGHT GAINS WERE RECORDED FOR ALL ANIMALS DURING THE COURSE OF THE STUDY.

TEST COMPOUND (VARISOFT 222-907 LOT NO. V2010225, 1% W/V): EIGHT OF THE ANIMALS WERE OBSERVED WITH SLIGHT TO MODERATE ERYTHEMA REACTIONS DURING THE SENSITIZING PHASE OF THE STUDY. SLIGHT EDEMA REACTIONS WERE EXHIBITED BY SIX ANIMALS FOLLOWING THE SENSITIZING APPLICATIONS. TWO ANIMALS (NOS. 64100020 AND 64100023) DID NOT EXHIBIT ANY ERYTHEMA REACTION AND FOUR ANIMALS (NOS. 64100016, 64100020, 64100022 AND 64100023) DID NOT EXHIBIT ANY EDEMA REACTIONS DURING THE SENSITIZING PHASE OF THE STUDY.

NONE OF THE ANIMALS IN THE TEST OR NAIVE CONTROL GROUP EXHIBITED EITHER AN ERYTHEMA OR EDEMA RESPONSE TO THE TEST MATERIAL FOLLOWING THE CHALLENGE APPLICATION WITH 0.5 ML OF A 1.0% W/V MIXTURE OF TEST MATERIAL IN STERILE 0.9% SALINE.

CONCLUSION: THIS TEST MATERIAL IS NOT CONSIDERED A SKIN SENSITIZER IN GUINEA PIGS BY THE CLOSED PATCH TECHNIQUE.

Dermal Sensitization In Guinea Pigs - Body Weights

☒ Test Group RT No. 816079 Vehicle 0.9% Saline Test Compound 816079
☐ Positive Control Group NA Vehicle NA ^{Sterile}

Animal Number								Tech- nician	Date 198
6410- 0016	6410- 0017	6410- 0018	6410- 0019	6410- 0020	6410- 0021	6410- 0022	6410- 0023		
444	447	467	473	501	444	505	485	NA SW	1/26
508	485	506	533	504	498	576	547	NA	2/2
557	522	556	582	551	550	635	614	NA	2/9
639	581	610	650	558	621	691	684	SW	2/16
718	761	675	702	608	710	758	771	NA	2/23
NA									

		Animal Number		
10410-0024	10410-0025		Tech-nician	Date
				1981
520	489	Scale Used: K-Tron 4809	ND SW	1/26
612	549	Scale Used: K-Tron 4809	NA	2/2
706	623	Scale Used: K-Tron 4809	ND	2/9
740	681	Scale Used: K-Tron 4809	SW	2/16
851	769	Scale Used: Penn 37.28	ND	2/23
NA	NA	Scale Used: NA	NA	NA

NA - Not Applicable

Dermal Sensitization In Guinea Pigs - Body Weights

☐ NA

Test Group RT No. 816079

Vehicle 0.9% Saline

Test Compound

Varisoft 222-C

LOT NO. V2010229

☒

Naive Untreated Control

Sterile

(190 wlv)

Animal Number								Tech- nician	Date 1981
6410-0026	6410-0027	6410-0028	6410-0029						
484	497	474	486					NJA Sw	1/26
553	588	560	562					NH	2/2
624	642	622	637					NJA	2/19
692	702	691	733					Sw	2/16
768	762	751	808					NJA	2/23
NA									

Animal Number								Tech- nician	Date 1981
								NJA Sw	1/26
								NH	2/2
								NJA	2/19
								Sw	2/16
								NJA	2/23

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Naive
☐ Untreated Control RT No. 8116079 Vehicle 0.9% Saline
Sterile

Date Animal Received 11/16/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6410-0026	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410-0027	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410-0028	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
6410-0029	0.5	NA			JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222- LOT NO. V20102 (1% w/v)
☒ Positive Control Group NA Vehicle NA Animal No. 6410-0025

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	TP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	TP	TP	1/30
		24	1.0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	1.0	0	ND	SG	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	1.0	1.0	ND	ND	2/5
		48	1.0	1.0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 811079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222- LOT NO. V2010Z (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0025

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	2.0	1.0	NA	JP	2/7
		48	2.0 D	0	JP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	0	NA	SW	2/10
		48	1.0	0	Bo	Bo	2/11
8	0.5	NA	NA	NA	USA	USA	2/11
		24	1.0	0	JP	JP	2-12
		48	1.0	0	JP	SW	3/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	JP	JP	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

D = desquamation
6/8/81 NA

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222- LOT NO. V20102 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0024
 Date Animal Received 1/16/81 Date Initiated 1/26/81
 Source Dean Daul Sex ♂ Challenge Date 2/27/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NDA	CD	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NDA	NDA	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8110079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222- LOT NO. V201077 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0024

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Dau1 Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	2.0	1.0	NDX	TP	2/7
		48	1.0	1.0	TP	NA	2/8
7	0.5	NA	NA	NA	R	R	2/9
		24	2.0	1.0	NDX	SW	2/10
		48	1.0 D	1.0	R	R	2/11
8	0.5	NA	NA	NA	NA	NA	2/11
		24	1.0 D	1.0	TP	JR	2-12
		48	1.0 D	0	TP	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	1.0 D	0	HH	HH	2/14
		48	1.0 D	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	TP	TP	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

D = DISQUALIFICATION
 CO 2/11/81

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Sterile Test Material Varisof 222-LOT NO. V20102 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0023

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Deon Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	TH	SW	1/27
		48	0	0	TH	TH	1/28
2	0.5	NA	NA	NA	TH	TH	1/28
		24	0	0	TH	TH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	TH	TH	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NA	CO	2/4
5	0.5	NA	NA	NA	TH	TH	2/4
		24	0	0	NA	NA	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816079

Vehicle 0.9% Saline Sterile

Test Material Varisof 222-9 LOT NO. V201072 (1% w/v)



Positive Control Group

NA

Vehicle

NA

Animal No. 6410-0023

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Daul

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	NDX	YYP	2/7
		48	0	0	YYP	NDX	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NDX	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	NDX	NDX	2/11
		24	0	0	YYP	JP	2-12
		48	0	0	YYP	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	HH	HH	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	YYP	YYP	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8110079 Vehicle 0.9% Saline Sterile Test Material Varisof 222- LOT NO. V20102 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0022

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Dawl Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NOX	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NOX	NOX	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated
NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Test Material Varisoft 222-1
Sterile (1% w/v)

☒ Positive Control Group NA Vehicle NA Animal No. 6410-0022

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Deon Dau Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	0	WJ	WJ	2/7
		48	0	0	WJ	WJ	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NJA	SW	2/10
		48	0	0	GO	GO	2/11
8	0.5	NA	NA	NA	NJA	NJA	2/11
		24	0	0	WJ	JP	2/12
		48	0	0	WJ	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	HH	HH	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	WJ	WJ	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8110079 Vehicle 0.9% Saline Sterile Test Material Varisof 222-LOT NO. V20102 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0021

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	1.0	0	JP	JP	1/31
		48	1.0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NTR	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	1.0	0	NTR	NTR	2/5
		48	1.0	0	SG	SG	2/6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8110079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222- LOT NO. V201027 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0021
 Date Animal Received 1/16/81 Date Initiated 1/26/81
 Source Dean Daul Sex ♂ Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	1.0	NDP	NDP	2/7
		48	1.0	0	NDP	NDP	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	0	NDP	SW	2/10
		48	1.0	0	CO	CO	2/11
8	0.5	NA	NA	NA	NDP	NDP	2/11
		24	1.0	0	NDP	JP	2/12
		48	0	0	NDP	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	NDP	NDP	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	NDP	NDP	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8116079

Vehicle 0.9% Saline
Sterile

Test

Varisof 222

Material

LOT NO. V20102

(1% w/v)



Positive Control Group

NA

Vehicle

NA

Animal No. 6410-

0020

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Dau1

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	TP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	TP	TP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	ND	CO	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	ND	ND	2/5
		48	0	0	SG	SG	2-6

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Sterile Test Material Varisoft 222 LOT NA V2010 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0020

Date Animal Received 1/16/81

Source Dean Dau Sex ♂

Date Initiated 1/26/81

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	NA	NA	2/7
		48	0	0	NA	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	NA	NA	2/11
		24	0	0	NA	JP	2/12
		48	0	0	NA	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	NA	NA	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 811079 Vehicle 0.9% Saline Sterile Test Material Varisof 222-LOT NO. V20102 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0019

Date Animal Received 1/16/81

Source Dean Dawl Sex ♂

Date Initiated 1/26/81

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NDA	SW	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NDA	NDA	2/5
		48	0	0	SG	SG	2-6

^a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8116079 Vehicle 0.9% Saline Sterile Test Material Varisof 222 LOT NA V2010 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0019

Date Animal Received 1/16/81

Date Initiated 1/26/81

Source Dean Daul Sex ♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	0	0	NTA	YP	2/7
		48	0	0	YP	NTA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	1.0	1.0	NTA	SW	2/10
		48	1.0	0	CO	CO	2/11
8	0.5	NA	NA	NA	NTA	NTA	2/11
		24	0	0	YP	JP	2/12
		48	0	0	YP	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	HH	HH	2/14
		48	0	0	SG	SG	2/15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	YP	YP	3/1

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 811079 Vehicle 0.9% Saline Sterile Test Material Varisof 222 LOT NO. V2010 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 4410-0018

Date Animal Received 1/16/81
 Source Dean Dawl Sex ♂

Date Initiated 1/26/81
 Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
1	0.5	NA	NA	NA	HN	HN	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HN	HN	1/28
2	0.5	NA	NA	NA	HN	HN	1/28
		24	0	0	HN	HN	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HN	HN	2/3
		48	0	0	NJA	CO	2/4
5	0.5	NA	NA	NA	HN	HN	2/4
		24	0	0	NJA	NJA	2/5
		48	0	0	SG	SG	2/6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816079

Vehicle 0.9% Saline
Sterile

Test

Varisof 222-

Material

LOT NO. V20102

(1% w/v)



Positive Control Group

NA

Vehicle

NA

6410-

Animal No. 0018

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Daul

Sex

♂

Challenge Date 2/27/81

Sensitizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	0	NA	NA	2/7
		48	1.0	1.0	TP	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CS	CS	2/11
8	0.5	NA	NA	NA	NA	NA	2/11
		24	0	0	TP	JP	2/12
		48	0	0	TP	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2/15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	4/8
		48	0	0	TP	TP	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 816079 Vehicle 0.9% Saline Sterile Test Material Varisof 222 LOT NA V2010 (1% w/v)
☐ Positive Control Group NA Vehicle NA Animal No. 6410-0017

Date Animal Received 1/16/81
 Source Dean Dawl Sex ♂

Date Initiated 1/26/81
 Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HH	HH	1/26
		24	0	0	JP	SW	1/27
		48	0	0	HH	HH	1/28
2	0.5	NA	NA	NA	HH	HH	1/28
		24	0	0	HH	HH	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	1.0	0	JP	JP	1/31
		48	1.0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	0	0	HH	HH	2/3
		48	0	0	NA	NA	2/4
5	0.5	NA	NA	NA	HH	HH	2/4
		24	0	0	NA	NA	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No.

816079

Vehicle

0.9% Saline
Sterile

Test

Varisoft 222

Material

LOT NO. V2010
(1% w/v)



Positive Control Group

NA

Vehicle

NA

Animal No.

6410-
0017

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Dawl

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Obser- vation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/16
		24	1.0	1.0	ND	ND	2/17
		48	0	0	ND	ND	2/18
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	ND	SW	2/10
		48	0	0	CD	CD	2/11
8	0.5	NA	NA	NA	ND	ND	2/11
		24	0	0	ND	JP	2-12
		48	1.0	0	ND	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	HN	HN	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	ND	ND	3/1

a - Dosage applied by technician indicated

NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8116079 Vehicle 0.9% Saline Sterile Test Material Varisof 222 LOT NO. V2010 (1% w/v)

☐ Positive Control Group NA Vehicle NA Animal No. 6410-0016

Date Animal Received 1/16/81

Source Dean Daul Sex ♂

Date Initiated 1/26/81

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
1	0.5	NA	NA	NA	HN	HN	1/26
		24	0	0	SW	SW	1/27
		48	0	0	HN	HN	1/28
2	0.5	NA	NA	NA	HN	HN	1/28
		24	0	0	HN	HN	1/29
		48	0	0	SW	SW	1/30
3	0.5	NA	NA	NA	JP	JP	1/30
		24	0	0	JP	JP	1/31
		48	0	0	JP	JP	2/1
4	0.5	NA	NA	NA	JP	JP	2/2
		24	1.0	0	HN	HN	2/3
		48	1.0	0	MTD	CO	2/4
5	0.5	NA	NA	NA	HN	HN	2/4
		24	1.0	0	MTD	MTD	2/5
		48	1.0	0	SG	SG	2-6

a - Dosage applied by technician indicated
 NA - Not Applicable

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 816079

Vehicle 0.9% Saline
Sterile

Test Material Varisof 222
LOT NO. V2010
(1% w/v)



Positive Control Group

NA

Vehicle

NA

Animal No. 6410-
0016

Date Animal Received

1/16/81

Date Initiated 1/26/81

Source

Dean Dawl

Sex

♂

Challenge Date 2/27/81

Sensi- tizing Dose No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6	0.5	NA	NA	NA	SW	SW	2/6
		24	1.0	0	NA	NA	2/7
		48	0	0	NA	NA	2/8
7	0.5	NA	NA	NA	JP	JP	2/9
		24	0	0	NA	SW	2/10
		48	0	0	CO	CO	2/11
8	0.5	NA	NA	NA	NA	NA	2/11
		24	0	0	NA	JP	2-12
		48	0	0	NA	SW	2/13
9	0.5	NA	NA	NA	SW	SW	2/13
		24	0	0	NA	NA	2/14
		48	0	0	SG	SG	2-15
Challenge Dose	0.5	NA	NA	NA	JP	JP	2/27
		24	0	0	JP	JP	2/28
		48	0	0	NA	NA	3/1

a - Dosage applied by technician indicated

NA - Not Applicable



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Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

ATT #50

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90%
(LOT NO. V2010225)

SPONSOR: SHEREX CHEMICAL COMPANY
DUBLIN, OH 43017

STUDY NO. 816079
INITIATION: 1/5/81
COMPLETION: 1/29/81
REPORTED: 2/24/81

SAMPLE: Varisoft 222-90% (Lot No. V2010225)

ENCLOSED: METHOD, PAGE 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
HEAD, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.



HAZLETON RALTECH, INC.

3301 KINSMAN BLVD. • P.O. BOX 7545 • MADISON, WISCONSIN 53707 • PHONE (608) 241-4471 • TLX 260098 HAZRAL MDS

Guinea Pig Maximization Study
Test Material Varisoft 222-90% (Lot No. V2010225)
Study No. 816079

Sponsor

Sherex Chemical Company
P. O. Box 646
Dublin OH 43017

Contractor

Hazleton Raltech, Inc.
3301 Kinsman Boulevard
Madison WI 53704

Principal Investigator

Robert L. Harrison

Study Director

Gary W. Thompson, BS

Amendment No. 1 to the Report

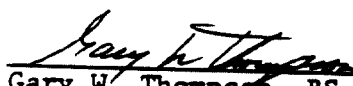
Reason

The stated volume of the dose was incorrect and the method of application of the test substance during intradermal injections was not clarified in the "Method" section of the final report.

Change

The Method section on page 2 of the final report, sentence 2, should be corrected to read:

"...one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material and Freund's Adjuvant Solution."



Gary W. Thompson, BS
Study Director, Acute Toxicology

6-4-82

Date

by and for Hazleton Raltech, Inc.

/dka



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Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

RT LAB NUMBER 816079
GUINEA PIG MAXIMIZATION

PAGE 2

Test Material: Varisoft 222-90% (Lot No. V2010225)

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for a conditioning period of at least 7 days.

Test System: Ten male guinea pigs weighing between 458 and 496 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 mL of sterile water for injection in 1.0 mL increments to 5.0 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.5 gram of Varisoft 222-90% (Lot No. V2010225) and adding sterile water for injection to a total volume of 10.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by placing 0.5 g of Varisoft 222-90% (Lot No. V2010225) into a 30-mL beaker and adding sterile water to a Q.S. volume of 5.0 mL. To this, 5.0 mL of Freund's Adjuvant was added in 1.0 mL increments while stirring.

For the topical induction the Varisoft 222-90% (Lot No. V2010225) was administered at a concentration of 50% w/v in sterile saline. For the challenge procedure, the test material was administered at a 1.0% w/v concentration in sterile saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.1 mL of the prepared Freund's Adjuvant Solution, 0.1 mL of a 5% aqueous test solution, and 0.1 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 50% w/v solution of Varisoft 222-90% (Lot No. V2010225) and sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.



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RT LAB NUMBER 816079
GUINEA PIG MAXIMIZATION

PAGE 3

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and shaving as before. A 1.0% w/v solution of the test material in sterile 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24-hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.



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Other Raltech Scientific Services Laboratories:
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RT LAB NUMBER 816079
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs
Source: Dean Dahl, Luxemburg, Wisconsin
Date Animals Received: 12/23/80

Test Material: Varisoft 222-90% (Lot No. V2010225)

Date Test Started: 1/5/81

Date Test Completed: 1/29/81

Animal Number	Sex	Challenge Dose Reactions	
		24 Hours	48 Hours
64000730	M	0	0
64000731	M	0	0
64000741	M	0	0
64000746	M	0	0
64000750	M	0	0
64000751	M	0	0
64000752	M	0	0
64000754	M	0	0
64000757	M	0	0
64000759	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90% (Lot No. V2010225):

None of the ten guinea pigs exhibited a reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90% (Lot No. V2010225), is not considered a skin sensitizer.

Reference:

Magnusson, B., MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 816079 Vehicle NA

Test Compound Varisoft
222-9070 LOT NO
V201022



Positive Control Group NA Vehicle NA

Animal Number								Tech- nician	Date
6400- 0730	6400- 0731	6400- 0741	6400- 0746	6400- 0750	6400- 0751	6400- 0752	6400- 0754		
474	491	460	459	478	490	496	489	ND	1/5/81
516	553	520	502	515	549	536	532	JP	1/16/81
518	538	518	476	505	568	526	532	SW	1/19/81
572	635	595	545	597	652	604	662	SW	1/26/81

		Animal Number	Tech- nician	Date
6400- 0757	6400- 0759			
458	470	Scale Used: K-TRON 4809	NJR	1/5/81
480	508	Scale Used: K-Tron 4809	JP	1/6/81
465	542	Scale Used: K-Tron 4809	SW	1/17/81
533	599	Scale Used: K-Tron 4809	SW	1/26/81
		Scale Used:		
		Scale Used:		

NA - Not Applicable

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-9076 LOT NO.
42010225

RT No. 8116079

pH Result NA

Sponsor No. N/A

Date Animals Received 12/23/80

Source Dean Dahl

Date of Intradermal Injections 1/5/81

Technician YD

Date of Topical Application 1/12/81

Technician GO INN

Date of Challenge 1/26/81

Technician INN

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
0400-0730 ♂	0		0	
0731 ♂	0		0	
0741 ♂	0		0	
0746 ♂	0		0	
0750 ♂	0		0	
0751 ♂	0		0	
0752 ♂	0		0	
0754 ♂	0		0	
0757 ♂	0		0	
0759 ♂	0		0	
Technician	YD		YD	
Recorded By	YD		YD	
Date 1981	Y28		Y29	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: _____

DATE: _____

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ X

Test Group RT No. 8116079 Vehicle N/A

Test Compound VariSoft 222

☒ N/A

Positive Control Group N/A Vehicle N/A

Room No. 1161 B *

LOT NO. 02010225

Animal Number								Technician	Date
6400-0730	6400-0731	6400-0741	6400-0746	6400-0750	6400-0751	6400-0752	6400-0754		
N	N	N	N	N	N	N	N	TP	1-5
N	N	N	N	N	N	N	N	TP	1-6
N	N	N	N	N	N	N	N	TP	1-7
N	N	N	N	N	N	N	N	TP	1-8
N	N	N	N	N	N	N	N	TP	1-9
N	N	N	N	N	N	N	N	TP	1-10
N	N	N	N	N	N	N	N	TP	1-11
N	N	N	N	N	N	N	N	TP	1-12
N	N	N	N	N	N	N	N	TP	1-13
N	N	N	N	N	N	N	N	TP	1-14
N	N	N	N	N	N	N	N	TP	1-15
N	N	N	N	N	N	N	N	TP	1-16
N	N	N	N	N	N	N	N	TP	1-17
N	N	N	N	N	N	N	N	TP	1-18
N	N	N	N	N	N	N	N	TP	1-19
N	N	N	N	N	N	N	N	TP	1-20
N	N	N	N	N	N	N	N	TP	1-21
N	N	N	N	N	N	N	N	TP	1-22

S = Excess Salivation 11/7/81 H14

N - No Visible Abnormalities

N/A - Not Applicable

* Test animals moved to room 3 on 11/5/81 N/A

Dermal Sensitization in Guinea Pigs - Daily Observations



Test Group RT No. 816079 Vehicle NA Test Compound Varisoft 222-90



Positive Control Group NA Vehicle NA Lot No. V2010225
Room No. 11/13

Animal Number								Tech- nicians	Date
6400-0757	6400-0759								1981
N	N							TP	1/5
N	N							JP	1/6
N	N							TP	1/7
N	N							NH	1/8
N	N							SG	1/9
N	N							CA	1/10
N	N							CA	1/11
N	N							JP	1/12
N	N							SG	1/13
N	N							SW	1/14
N	N							NH	1/15
N	N							SW	1/16
N	N							NH	1/17
N	N							NH	1/18
N	N							SW	1/19
N	N							JP	1/20
N	N							SG	1-21
N	N							TP	1/22

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 1/15/81 NJO

Dermal Sensitization in Guinea Pigs - Daily Observations

Room No. 1106 G A

[illegible]

N - No Visible Abnormalities.

NA - Not Applicable

* Test animals moved to room 3 on 11/15/81 NDD

Dermal Sensitization in Guinea Pigs - Daily Observations

Test Group RT No. 816079 Vehicle 110 Test Compound Varisoft 222
Positive Control Group 110 Vehicle 110 LOT NO. V2010225
Room No. 1101B *

Positive Control Group 110 Vehicle 110 LOT NO. V2010225
Room No. 1101 B

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

* Test animals moved to room 3 on 11/5/81 NJN



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Other Raltech Scientific Services Laboratories:
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AT 750

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90
LOT #SC49-66A 644750

SPONSOR: SHEREX CHEMICAL COMPANY
DUBLIN, OHIO

STUDY NO. 856938
INITIATION: 4/27/81
COMPLETION: 5/21/81
REPORTED: 6/3/81

SAMPLE: VARISOFT 222-90 LOT #SC49-66A 644750

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot #SC49-66A 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 448 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-66A 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by mixing 0.25 g of Varisoft 222-90 Lot #SC49-66A 644750 with 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1.0 mL increments to a total volume of 5.0 mL.

For the topical induction and challenge procedures the test material was applied at 25% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 25% w/v suspension of test material in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs
Source: Dean Daul, Luxemburg, WI
Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-66A 644750

Date Test Started: 4/27/81

Date Test Completed: 5/21/81

<u>Animal Number</u>	<u>Sex</u>	<u>24 Hours Right</u>	<u>48 Hours Right</u>
64100216	M	1	0
64100217	M	0	0
64100218	M	0	0
64100219	M	0	0
64100220	M	0	0
64100221	M	0	0
64100222	M	0	0
64100223	M	1	0
64100224	M	0	0
64100225	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for five animals during the course of the study. Four guinea pigs exhibited a weight loss and one animal exhibited a slight weight gain at the end of the second week on test. Normal body weight gains were recorded for these animals at the one and three week weighings.

Skin Reactions to Varisoft 222-90 Lot #SC49-66A 644750:

Two animals (Nos. 64100216 and 64100223) exhibited a sensitization reaction to the test material at 24 hours following the challenge application. Both animals had a scattered mild redness of the test site at 24 hours. Eight guinea pigs did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-66A 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

Test Compound Pharisol 222-90
 LOT # SC49-66A644750
 pH Result NA
 Date Animals Received 4/10/81
 Date of Intradermal Injections 4/27/81
 Date of Topical Application 5/4/81
 Date of Challenge 5/18/81

RT No. 856938
 Sponsor No. NA
 Source Dean Dowl
 Technician SW, TP, NDA
 Technician NDA
 Technician NDA ER

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6410- 0216 ♂	1		0	
0217 ♂	0		0	
0218 ♂	0		0	
0219 ♂	0		0	
0220 ♂	0		0	
0221 ♂	0		0	
0222 ♂	0		0	
0223 ♂	1		0	
0224 ♂	0		0	
0225 ♂	0		0	
Technician	Co		TP	
Recorded By	ER		TP	
Date 1981	5/20		5/21	

NA - Not Applicable
 4/27/81 NDA

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: NDA DATE: 5/29/81

Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 856938

Vehicle NA

Test Compound VORASO 222-4



Positive Control Group NA

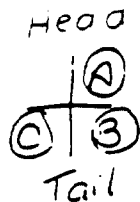
Vehicle NA

LOT # SC 49-66A
644750

Animal Number								Technician	Date
640-	640-	640-	640-	6410-	6410-	6410-	6410-		
0216	0217	0218	0219	0220	0221	0222	0223		
498	456	496	500	475	477	448	448	ND	4/27/81
514	517	584	559	524	532	498	499	MP	5/4/81
569	522	626	562	521	543	478	534	MP	5/11/81
770	618	691	658	637	628	573	619	JP ND	5/18/81

		Animal Number		Technician	Date
640-	640-				
0224	0225				
459	460	Scale Used: K-TRON 4809		ND	4/27/81
528	512	Scale Used: K-TRON 4809		MP	5/4/81
509	473	Scale Used: K-TRON 4809		MP	5/11/81
595	593	Scale Used: K-TRON 4809		JP ND	5/18/81
		Scale Used:			
		Scale Used:			

NA - Not Applicable



Dose Range
DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 856938 Vehicle Sterile 0.9% Saline Test Material Varisolt 222-90
 LOT # SC 49-66A 644750

Date Animal Received 4/3/81

Source Dean Dawl Sex ♂

Date Initiated 4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0129 ①	0.5	NA	NA	NA	NJD	ER	4/23
	1.0%	24	0	0	JP	JP	4/24
		48	0	0	JP	JP	4/25
0129 ②	0.5	NA	NA	NA	NJD	ER	4/23
	5.0%	24	1.0	1.0	JP	JP	4/24
		48	1.0	1.0	JP	JP	4/25
0129 ③	0.5	NA	NA	NA	NJD	ER	4/23
	10.0%	24	2.0	1.0	JP	JP	4/24
		48	1.0	1.0	JP	JP	4/25
0129 ④	10.0%	NA	NA	NA		① ER	① 4/23
		24					
		48					
0129 ⑤	10.0%	NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated

NA - Not Applicable

① recording error 4/23/81 ER

Head
 (A)
 (C) (B)
 Tail

Dose Range
DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9% Saline

Test

Material Varisalt 222
 LOT # SC-4966A644

Date Animal Received 4/13/81

Source Dean Daul Sex ♂

Date Initiated 4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0183 (A)	0.5	NA	NA	NA	NDP	NDP	4/23
	10.0%	24	1.0	1.0	NDP	NDP	4/24
		48	1.0	1.0	JP	JP	4/25
0183 (B)	0.5	NA	NA	NA	NDP	NDP	4/23
	1.0%	24	0	0	NDP	NDP	4/24
		48	0	0	JP	JP	4/25
0183 (C)	0.5	NA	NA	NA	NDP	NDP	4/23
	5.0%	24	2.0	2.0	NDP	NDP	4/24
		48	2.0	1.0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Head
 (A)
 (B)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Test

Material Varisof+ 232-90

Saline

LOT# SC49-66964475

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

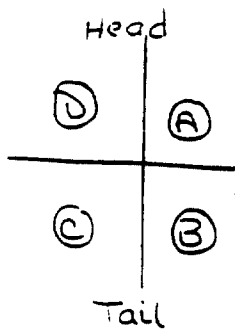
Date Initiated

4/33/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0182 (A)	0.5	NA	NA	NA	NDV	NDV	4/23
	5.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0182 (B)	0.5	NA	NA	NA	NDV	NDV	4/23
	10.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0182 (C)	0.5	NA	NA	NA	NDV	NDV	4/23
	1.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Test

Material Uniscript 222-90

Saline

LOT # SC 49-66A 64478

Date Animal Received

4/13/81

Source

Dean Daul

Sex

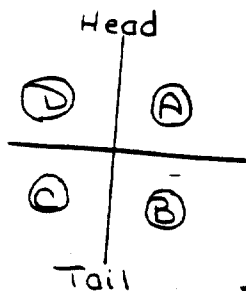
♂

Date Initiated

4/21/81

Animal No. SITE	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0156	0.5	NA	NA	NA	NDA	ER	4/21
(A)	25%	24	0	0	CO	NDA	4/22
		48	2.0	1.0	NDA	NDA	4/23
0156	0.5	NA	NA	NA	NDA	ER	4/21
(B)	50%	24	2.0	2.0	CO	NDA	4/22
		48	2.0	2.0	NDA	NDA	4/23
0156	0.5	NA	NA	NA	NDA	ER	4/21
(C)	75%	24	2.0	3.0	CO	NDA	4/22
		48	2.0	3.0	NDA	NDA	4/23
0156	0.5	NA	NA	NA	NDA	ER	4/21
(D)	100%	24	2.0	3.0	CO	NDA	4/22
		48	2.0	3.0	NDA	NDA	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9% Saline

Test

Material Varisaf + 222-90
LOT # SC 49-66A64475

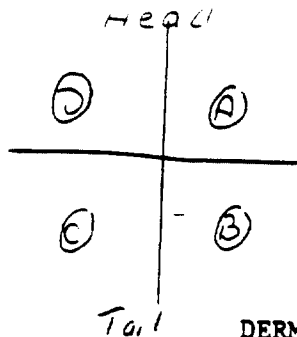
Date Animal Received 4/3/81

Source Dean Daul Sex ♂

Date Initiated 4/2/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0119 A	0.5	NA	NA	NA	NJA	ER	4/21
	100%	24	2.0	3.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
0119 B	0.5	NA	NA	NA	NJA	ER	4/21
	25%	24	1.0	0	CO	NJA	4/22
		48	2.0	1.0	NJA	NJA	4/23
0119 C	0.5	NA	NA	NA	NJA	ER	4/21
	50%	24	2.0	2.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
0119 D	0.5	NA	NA	NA	NJA	ER	4/21
	75%	24	2.0	2.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9% Saline Test Material Vol. 50 of 222-90 LOT = SC 49-66A644750

Date Animal Received 4/13/81

Source Dean Paul

Sex ♂

Date Initiated 4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0143 A	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	GO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0143 B	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	GO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0143 C	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	1.0	0	GO	NDX	4/22
		48	2.0	1.0	NDX	NDX	4/23
0143 D	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	GO	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Test

Material Varisoft 222-90

Saline

LOT # SC 49-66A644750

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No. <u>Site</u>	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0144 A	0.5	NA	NA	NA	NDN	ER	4/21
	50%	24	2.0	2.0	CO	NDN	4/22
		48	2.0	3.0	NDN	NDN	4/23
0144 B	0.5	NA	NA	NA	NDN	ER	4/21
	75%	24	2.0	3.0	CO	NDN	4/22
		48	2.0	3.0	NDN	NDN	4/23
0144 C	0.5	NA	NA	NA	NDN	ER	4/21
	100%	24	2.0	3.0	CO	NDN	4/22
		48	2.0	3.0	NDN	NDN	4/23
0144 D	0.5	NA	NA	NA	NDN	ER	4/21
	25%	24	2.0	0	CO	NDN	4/22
		48	2.0	2.0	NDN	NDN	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head
 (A)
 (C) (B)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9% Saline

Test

Material Varisolt 222-90
 LOT # SC 49-669644750

Date Animal Received

4/3/81

Source

Deane Daul

Sex

♂

Date Initiated

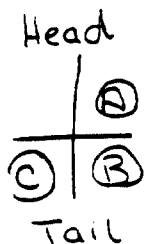
4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0129 (A)	0.5	NA	NA	NA	NDP	ER	4/23
	1.0%	24	0	0	NDP	NDP	4/24
		48	0	0	TR	TR	4/25
0129 (B)	0.5	NA	NA	NA	NDP	ER	4/23
	5.0%	24	1.0	1.0	NDP	NDP	4/24
		48	1.0	1.0	TR	TR	4/25
0129 (C)	0.5	NA	NA	NA	NDP	ER	4/23
	10.0%	24	2.0	1.0	NDP	NDP	4/24
		48	1.0	1.0	TR	TR	4/25
 		NA	NA	NA		①	① 4/23
		24				ER	
		48					
 		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① recording error 4/23/81 ER



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group: RT No. 856938 Vehicle Sterile 0.9% Saline Test Material Varisoft 222-90 LOT # SC-4966A6475C

Date Animal Received 4/3/81

Source Dean Daul Sex ♂

Date Initiated 4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0183 (A)	0.5	NA	NA	NA	NDP	NDP	4/23
		24	1.0	1.0	NDP	NDP	4/24
		48	1.0	1.0	JP	JP	4/25
0183 (B)	0.5	NA	NA	NA	NDP	NDP	4/23
		24	0	0	NDP	NDP	4/24
		48	0	0	JP	JP	4/25
0183 (C)	0.5	NA	NA	NA	NDP	NDP	4/23
		24	2.0	2.0	NDP	NDP	4/24
		48	2.0	1.0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

- Dosage applied by technician indicated

A - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Test

Material Varsoft 27.9

Saline

LOT# SC49-662644

Date Animal Received

4/3/81

Source

Debn Daul

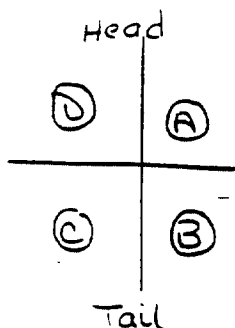
Sex

Date Initiated

4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0182 ②	0.5	NA	NA	NA	NDV	NDV	4/23
	5.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0182 ③	0.5	NA	NA	NA	NDV	NDV	4/23
	10.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0182 ④	0.5	NA	NA	NA	NDV	NDV	4/23
	1.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Saline

Test

Material Varisoft 222-90

LOT # SC 49-66A 64473

Date Animal Received

4/13/81

Source

Dean Daul

Sex

♂

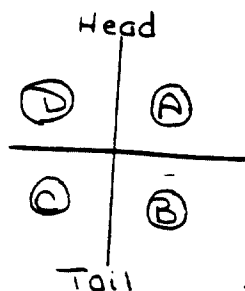
Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0156 (A)	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	0	0	CO	NDX	4/22
		48	2.0	1.0	NDX	NDX	4/23
0156 (B)	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
0156 (C)	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	3.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0156 (D)	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	3.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9% Saline

Test

Material Varisaf + 222-a

LOT # SC 49-66A6447

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

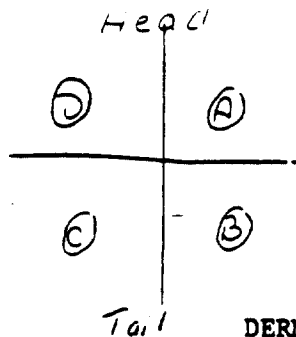
Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0119 (A)	0.5	NA	NA	NA	NJA	ER	4/21
	100%	24	2.0	3.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
0119 (B)	0.5	NA	NA	NA	NJA	ER	4/21
	25%	24	1.0	0	CO	NJA	4/22
		48	2.0	1.0	NJA	NJA	4/23
0119 (C)	0.5	NA	NA	NA	NJA	ER	4/21
	50%	24	2.0	2.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
0119 (D)	0.5	NA	NA	NA	NJA	ER	4/21
	75%	24	2.0	2.0	CO	NJA	4/22
		48	2.0	3.0	NJA	NJA	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Material Volisof + 222-90

Saline

Test

LOT # SC 49-66A644750

Date Animal Received

4/13/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0143 (A)	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0143 (B)	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0143 (C)	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	1.0	0	CO	NDX	4/22
		48	2.0	1.0	NDX	NDX	4/23
0143 (D)	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856938

Vehicle Sterile 0.9%

Saline

Test

Material Varisort 222-90

LOT # SC 49-66A6447

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0144 Ⓐ	0.5	NA	NA	NA	NJN	ER	4/21
	50%	24	2.0	2.0	CO	NJN	4/22
		48	2.0	3.0	NJN	NJN	4/23
0144 Ⓑ	0.5	NA	NA	NA	NJN	ER	4/21
	75%	24	2.0	3.0	CO	NJN	4/22
		48	2.0	3.0	NJN	NJN	4/23
0144 Ⓒ	0.5	NA	NA	NA	NJN	ER	4/21
	100%	24	2.0	3.0	CO	NJN	4/22
		48	2.0	3.0	NJN	NJN	4/23
0144 Ⓓ	0.5	NA	NA	NA	NJN	ER	4/21
	25%	24	2.0	0	CO	NJN	4/22
		48	2.0	2.0	NJN	NJN	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable



JUN 19 1981

Other Raltech Scientific Services Laboratories:
St. Louis MO
Gray Summit MO

P.O. Box 7545 • Madison, Wisconsin 53707 • 608/241-4471
A Division of Ralston Purina Company

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90
LOT #SC49-66B 644750

SPONSOR: SHEREX CHEMICAL CO.
DUBLIN, OHIO

STUDY NO. 856939
INITIATION: 4/27/81
COMPLETION: 5/21/81
REPORTED: 6/3/81

SAMPLE: VARISOFT 222-90 LOT #SC49-66B 644750

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot #SC49-66B 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 426 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-66B 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot #SC49-66B 644750 in 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1 mL increments to a total volume of 5.0 mL

For the topical induction and challenge procedures the Varisoft 222-90 Lot #SC49-66B 644750 was applied at 10% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 10% w/v suspension of Varisoft 222-90 in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs
Source: Dean Daul, Luxemburg, WI
Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-66B 644750

Date Test Started: 4/27/81

Date Test Completed: 5/21/81

<u>Animal Number</u>	<u>Sex</u>	<u>24 Hours Right</u>	<u>48 Hours Right</u>
64100226	M	0	0
64100227	M	1	1
64100228	M	1	0
64100229	M	1	1
64100230	M	1	1
64100231	M	1	0
64100232	M	0	0
64100233	M	0	0
64100234	M	0	0
64100235	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for seven animals during the course of the study. One animal (No. 64100234) exhibited a body weight loss, one animal showed no gain in body weight and one animal exhibited a slight body weight gain during the second week on test. These animals had normal body weight gains during the third week on test.

Skin Reactions to Varisoft 222-90 Lot #SC49-66B 644750:

Five animals exhibited a sensitization reaction to the test material following the challenge application. Each animal reacting to the challenge dose exhibited a mild redness at 24 hours and three of these animals continued to show a mild redness at the 48 hour observation. The other five animals did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-66B 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-90 Lot #5C 49-66B - RT No. 856939
 pH Result NA 644750 Sponsor No. NA
 Date Animals Received 4/10/81 Source Dean Daw
 Date of Intradermal Injections 4/27/81 Technician SW, MP, NTV
 Date of Topical Application 5/4/81 Technician NTV
 Date of Challenge 5/18/81 Technician NTV ER

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6410-0226 ♂	0		0	
0227 ♂	1		1	
0228 ♂	1		0	
0229 ♂	1		1	
0230 ♂	1		1	
0231 ♂	1		0	
0232 ♂	0		0	
0233 ♂	0		0	
0234 ♂	0		0	
0235 ♂	0		0	
Technician	CO		JP	
Recorded By	ER		JP	
Date 1981	5/20		5/21	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: NTV DATE: 5/29/81

① Maximization
Dermal Sensitization In Guinea Pigs - Body Weights



Test Group RT No. 856939 Vehicle NA

Test Compound Varisoft 222-9



Positive Control Group NA Vehicle NA

Lot # 5C 49-66B
644750

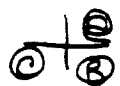
Animal Number								Tech- nician	1981 Date
6410- 0226	6410- 0227	6410- 0228	6410- 0229	6410- 0230	6410- 0231	6410- 0232	6410- 0233		
450	500	456	482	447	426	464	497	SW	4/27
514	651	516	532	483	481	518	559	JP	5/4
536	686	540	553	496	481	547	566	JP	5/11
633	781	633	600	583	595	621	662	JP	5/18

		Animal Number		
6410- 0234	6410- 0235		Tech- nician	1981 Date
468	495	Scale Used: K-Tron 4809	SW	4/27
518	583	Scale Used: K-Tron 4809	JP	5/4
405	637	Scale Used: K-Tron 4809	JP	5/11
564	722	Scale Used: K-TRON 4809	JP 100	5/18
		Scale Used:		
		Scale Used:		

① Farm Check

① Form Change SW 4/27/81

NA - Not Applicable

Head

 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939

Vehicle Sterile 0.9%

Test

Material Vari-Soft 222-9

Saline

LOT # SC 496686-4750

Date Animal Received 4/13/81

Source Dean Paul Sex ♂

Date Initiated 4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0410 - Site							1981
0186 A	0.5	NA	NA	NA	NDV	NDV	4/23
	1.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0186 B	0.5	NA	NA	NA	NDV	NDV	4/23
	5.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
0186 C	0.5	NA	NA	NA	NDV	NDV	4/23
	10.0%	24	2.0	1.0	NDV	NDV	4/24
		48	2.0	1.0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Head
 (C) (B)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939 Vehicle Stable 0.9% Test Material Varisoft 222-9
Saline LOT# SC 49-6686447

Date Animal Received 4/3/81

Source Dean Daul Sex ♂

Date Initiated 4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0410- Site							1981
0187 (A)	0.5	NA	NA	NA	NDN	NDN	4/23
	10.0%	24	2.0	1.0	NDN	NDN	4/24
		48	2.0	1.0	JP	JP	4/25
0187 (B)	0.5	NA	NA	NA	NDN	NDN	4/23
	1.0%	24	0	0	NDN	NDN	4/24
		48	0	0	JP	JP	4/25
0187 (C)	0.5	NA	NA	NA	NDN	NDN	4/23
	5.0%	24	1.0	1.0	NDN	NDN	4/24
		48	1.0	1.0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

lead
1/2
1/2
in

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No 856939

Vehicle Stable 0.9%

Test

Material Varisoft 222-90
Saline LOT # 5C49-660644750

Animal Received

4/3/81

Source

Dean Daul

Sex

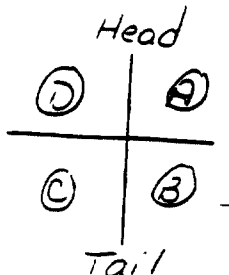
♂

Date Initiated

4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0							4/81
18	0.5	NA	NA	NA	NDP	NDP	4/23
19	5.0%	24	1.0	0	NDP	NDP	4/24
		48	1.0	0	JP	JP	4/25
20	0.5	NA	NA	NA	NDP	NDP	4/23
21	10.0%	24	2.0	1.0	NDP	NDP	4/24
		48	2.0	1.0	JP	JP	4/25
22	0.5	NA	NA	NA	NDP	NDP	4/23
	1.0%	24	0	0	NDP	NDP	4/24
		48	0	0	JP	JP	4/25
<hr/>							
		NA	NA	NA			
		24					
		48					
<hr/>							
		NA	NA	NA			
		24					
		48					

Dosage applied by technician indicated
Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939

Vehicle Sterile 0.9%

Test

Material Varisoft 222-90

Saline

LOT NO. SC 49-66B6447

Date Animal Received 4/3/81

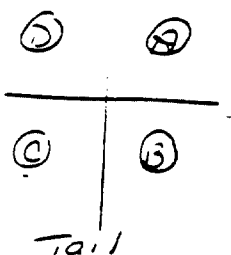
Source Dean Daul Sex ♂

Date Initiated 4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410- 0161 A	0.5	NA	NA	NA	NTD	ER	1981 4/21
	25%	24 48	1.0 2.0	0 1.0	CO	NTD	4/22 4/23
0161 B	0.5	NA	NA	NA	NTD	ER	4/21
	50%	24 48	2.0 2.0	1.0 2.0	CO	NTD	4/22 4/23
0161 C	0.5	NA	NA	NA	NTD	ER	4/21
	75%	24 48	2.0 2.0	2.0 3.0	CO	NTD	4/22 4/23
0161 D	0.5	NA	NA	NA	NTD	ER	4/21
	100%	24 48	2.0 3.0	3.0 3.0	CO	NTD	4/22 4/23
		NA	NA	NA			
		24 48					

^a - Dosage applied by technician indicated
NA - Not Applicable

Head



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8510939

Vehicle Sterile 0.9% Saline

Test

Material Varisot 1 222-90

LOT NO. SC 49-660644

Date Animal Received 4/13/81

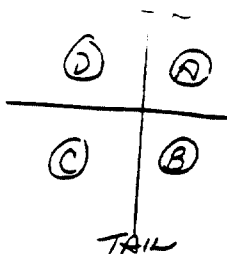
Source Deon Daul

Sex ♂

Date Initiated 4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0162 A	0.5	NA	NA	NA	NDX	SR	4/21
	100%	24	2.0	3.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0162 B	0.5	NA	NA	NA	NDX	SR	4/21
	25%	24	2.0	1.0	CO	NDX	4/22
		48	2.0	1.0	NDX	NDX	4/23
0162 C	0.5	NA	NA	NA	NDX	SR	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
0162 D	0.5	NA	NA	NA	NDX	SR	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939

Vehicle Sterile 0.9% Saline

Test

Material VariSoft 222-0

LOT NO. SC 49-66864

Date Animal Received

4/3/81

Source

Dean Dowl

Sex

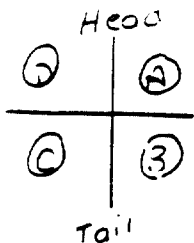
♂

Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0164 (A)	0.5	NA	NA	NA	NJN	ER	4/21/81
	75%	24	2.0	3.0	CS	NJN	4/22
		48	3.0	3.0	NJN	NJN	4/23
0164 (B)	0.5	NA	NA	NA	NJN	ER	4/21
	100%	24	2.0	2.0	CS	NJN	4/22
		48	3.0	3.0	NJN	NJN	4/23
0164 (C)	0.5	NA	NA	NA	NJN	ER	4/21
	25%	24	1.0	0	CS	NJN	4/22
		48	2.0	1.0	NJN	NJN	4/23
0164 (D)	0.5	NA	NA	NA	NJN	ER	4/21
	50%	24	2.0	1.0	CS	NJN	4/22
		48	2.0	2.0	NJN	NJN	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Test Group:

RT No.

851239

Vehicle

Sterile 0.9% Saline

Test

Material Varisole 222-90

LOT NO. SC49-68644750

Animal Received

4/13/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
03	0.5	NA	NA	NA	NDX	ER	4/21/81
2)	50%	24	2.0	2.0	NDX	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
03	0.5	NA	NA	NA	NDX	ER	4/21
3)	75%	24	2.0	3.0	NDX	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
03	0.5	NA	NA	NA	NDX	ER	4/21
4)	100%	24	2.0	3.0	NDX	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
03	0.5	NA	NA	NA	NDX	ER	4/21
5)	25%	24	2.0	1.0	NDX	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

Dosage applied by technician indicated

Not Applicable

according error 4/21/81 ER

Head

 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8510939

Vehicle Sterile 0.9% Saline

Test

Material Varisolt 22
 LOT # SC 49008644

Date Animal Received 4/13/81

Source Don Daw Sex ♂

Date Initiated 4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0410 - 0186 A	0.5	NA	NA	NA	NDV	NDV	4/23
	1.0%	24 48	0 0	0 0	NDV JP	NDV JP	4/24 4/25
0186 B	0.5	NA	NA	NA	NDV	NDV	4/23
	5.0%	24 48	0 0	0 0	NDV JP	NDV JP	4/24 4/25
0186 C	0.5	NA	NA	NA	NDV	NDV	4/23
	10.0%	24 48	2.0 2.0	1.0 1.0	NDV JP	NDV JP	4/24 4/25
		NA	NA	NA			
		24 48					
		NA	NA	NA			
		24 48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Head
 (C) (B)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939

Vehicle Stable 0.9%

Test

Material Varisof 222

Saline LOT# SC 49-66664

Date Animal Received 4/23/81

Source Dean Daul Sex ♂

Date Initiated 4/23/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0410-							1981
0187 (A)	0.5	NA	NA	NA	NDN	NDN	4/23
	10.0%	24	2.0	1.0	NDN	NDN	4/24
		48	2.0	1.0	JP	JP	4/25
0187 (B)	0.5	NA	NA	NA	NDN	NDN	4/23
	1.0%	24	0	0	NDN	NDN	4/24
		48	0	0	JP	JP	4/25
0187 (C)	0.5	NA	NA	NA	NDN	NDN	4/23
	5.0%	24	1.0	1.0	NDN	NDN	4/24
		48	1.0	1.0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
 NA - Not Applicable

Head
 ②
 ①/③
 Tail

Dose Range
DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No 851839

Vehicle Stable 0.9% Test

Material Varisoft 222.0

Saline LOT # SC49-660647

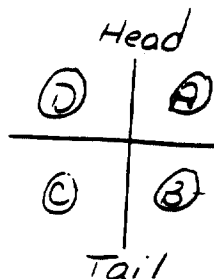
Date Animal Received 4/3/81

Source Dean Daul Sex ♂

Date Initiated 4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410							481
<u>Site</u>							
0188 ②	0.5	NA	NA	NA	NDV	NDV	4/23
	5.0%	24	1.0	0	NDV	NDV	4/24
		48	1.0	0	JP	JP	4/25
0188 ③	0.5	NA	NA	NA	NDV	NDV	4/23
	10.0%	24	2.0	1.0	NDV	NDV	4/24
		48	2.0	1.0	JP	JP	4/25
0188 ③	0.5	NA	NA	NA	NDV	NDV	4/23
	1.0%	24	0	0	NDV	NDV	4/24
		48	0	0	JP	JP	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939

Vehicle Sterile 0.9% Saline

Test

Material Varisoft 222-9
LOT NO. SC 49-668644

Date Animal Received 4/3/81

Source Dean Daul

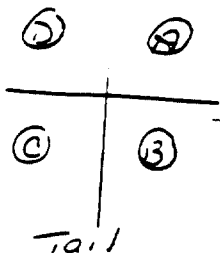
Sex ♂

Date Initiated 4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410- 0161 ①	0.5	NA	NA	NA	NDV	ER	4/21
	25%	24	1.0	0	CO	NDV	4/22
		48	2.0	1.0	NDV	NDV	4/23
0161 ②	0.5	NA	NA	NA	NDV	ER	4/21
	50%	24	2.0	1.0	CO	NDV	4/22
		48	2.0	2.0	NDV	NDV	4/23
0161 ③	0.5	NA	NA	NA	NDV	ER	4/21
	75%	24	2.0	2.0	CO	NDV	4/22
		48	2.0	3.0	NDV	NDV	4/23
0161 ④	0.5	NA	NA	NA	NDV	ER	4/21
	100%	24	2.0	3.0	CO	NDV	4/22
		48	3.0	3.0	NDV	NDV	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Head



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8516939

Vehicle Sterile 0.9% Saline

Test

Material Varisol 1 222-90

LOT NO. SL 49-660644

Date Animal Received 4/3/81

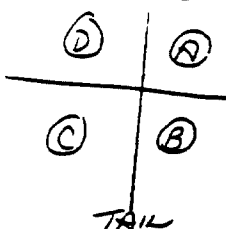
Source Dean Daul

Sex ♂

Date Initiated 4/21/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410							1981
0162	0.5	NA	NA	NA	NDX	SR	4/21
Ⓐ	100%	24	2.0	3.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
0162	0.5	NA	NA	NA	NDX	SR	4/21
Ⓑ	25%	24	2.0	4.0	CO	NDX	4/22
		48	2.0	4.0	NDX	NDX	4/23
0162	0.5	NA	NA	NA	NDX	SR	4/21
Ⓒ	50%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	2.0	NDX	NDX	4/23
0162	0.5	NA	NA	NA	NDX	SR	4/21
Ⓓ	75%	24	2.0	2.0	CO	NDX	4/22
		48	2.0	3.0	NDX	NDX	4/23
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
NA - Not Applicable



Dose 2-22

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856939 Vehicle Sterile 0.9% Saline Test Material Varisoft 222 LOT NO. SC 49-66B64

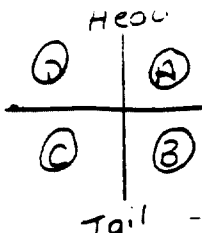
Date Animal Received 4/3/81

Source Dean Dowl Sex ♂

Date Initiated 4/2/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0164 (A)	0.5	NA	NA	NA	NJN	ER	4/21
	75%	24	2.0	3.0	CS	NJN	4/22
		48	3.0	3.0	NJN	NJN	4/23
0164 (B)	0.5	NA	NA	NA	NJN	ER	4/21
	100%	24	2.0	2.0	CS	NJN	4/22
		48	3.0	3.0	NJN	NJN	4/23
0164 (C)	0.5	NA	NA	NA	NJN	ER	4/21
	25%	24	1.0	0	CS	NJN	4/22
		48	2.0	1.0	NJN	NJN	4/23
0164 (D)	0.5	NA	NA	NA	NJN	ER	4/21
	50%	24	2.0	1.0	CS	NJN	4/22
		48	2.0	2.0	NJN	NJN	4/23
		NA	NA	NA			
		24					
		48					

^a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 851939

Vehicle Sterile 0.9% Saline

Test

Material Varisat 1 222-90

LOT NO. SC 49-68644750

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
							1981
0163 A	0.5 50%	NA	NA	NA	NXX	ER	4/21
		24	2.0	2.0	CO	NXX	4/22
		48	3.0	2.0	NXX	NXX	4/23
0163 B	0.5 75%	NA	NA	NA	NXX	ER	4/21
		24	2.0	3.0	CO	NXX	4/22
		48	2.0	3.0	NXX	NXX	4/23
0163 C	0.5 100%	NA	NA	NA	NXX	ER	4/21
		24	2.0	3.0	CO	NXX	4/22
		48	2.0	3.0	NXX	NXX	4/23
0163 D	0.5 25%	NA	NA	NA	NXX	ER	4/21
		24	2.0	1.0	CO	NXX	4/22
		48	2.0	2.0	NXX	NXX	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① recording error 4/21/81 ER



P.O. Box 7545 • Madison, Wisconsin 53707 • 608/241-4471

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GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90
LOT #SC49-68 644750

SPONSOR: SHEREX CHEMICAL CO.
DUBLIN, OHIO

STUDY NO. 856940
INITIATION: 4/27/81
COMPLETION: 5/21/81
REPORTED: 6/03/81

SAMPLE: VARISOFT 222-90 LOT #SC49-68 644750

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
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MANAGER, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot #SC49-68B 644750

Test Animal: Young adult male guinea pigs were procured, maintained individually in stainless steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 398 and 500 grams were chosen at random and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5 mL of sterile water for injection in 1 mL increments to 5 mL of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot #SC49-68 644750 and adding sterile water for injection to a total volume of 5.0 mL.

The 5% solution of test material in Freund's Adjuvant was prepared by mixing 0.25 g of Varisoft 222-90 Lot #SC49-68 644750 in 2.5 mL of sterile water and adding 2.5 mL of Freund's Adjuvant in 1.0 mL increments to a total volume of 5.0 mL.

For the topical induction and challenge procedures the Varisoft 222-90 Lot #SC49-68 644750 was applied at 10% w/v and 1.0% w/v suspensions in 0.9% saline, respectively.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 mL of the prepared Freund's Adjuvant Solution, 0.05 mL of a 5% aqueous test solution, and 0.05 mL of a 5% solution of test material and Freund's Adjuvant Solution.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 10% w/v suspension of Varisoft 222-90 in 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 1.0% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Pathology: Any animal that died during the course of the study was subjected to a gross necropsy examination and abnormalities recorded. At study termination all surviving animals were euthanatized and discarded.

Test Animal: Albino guinea pigs
Source: Dean Daul, Luxemburg, WI
Date Animals Received: 4/10/81

Test Material: Varisoft 222-90 Lot #SC49-68 644750

Date Test Started: 4/27/81

Date Test Completed: 5/21/81

<u>Animal Number</u>	<u>Sex</u>	<u>24 Hours Right</u>	<u>48 Hours Right</u>
64100236	M	0	0
64100237	M	-	-
64100238	M	0	0
64100239	M	1	0
64100240	M	0	0
64100241	M	0	0
64100242	M	3	2
64100243	M	1	0
64100244	M	0	0
64100245	M	0	0

General Behavior and Appearance:

One animal (No. 64100237) was found dead on 5/9/81. This animal was hypoactive and ataxic on 5/8/81. The only abnormality observed at necropsy was that the stomach was distended with gas and a reddish-brown liquid. This death is not considered treatment related. No signs of sytemic toxicity were observed in any of the remaining nine animals at any observation period during the study.

Normal body weight gains were recorded for four animals during the course of the study. One animal (No. 64100244) exhibited a body weight loss and four animals showed a slight body weight gain during the second week on test. Normal body weight gains were recorded for all animals at the end of the third week on test.

Skin Reactions to Varisoft 222-90 Lot #SC49-68 644750:

Three animals (Nos. 64100239, 64100242, and 64100243) exhibited a sensitization reaction to the test material following the challenge application. Two animals (Nos. 64100239 and 64100243) reacted with a mild redness at 24 hours and one animal (64100242) exhibited an intense redness and swelling at 24 hours and a moderate and diffuse redness at 48 hours. The six remaining animals did not exhibit any reaction to the challenge dose at either the 24 or 48 hour observations.

Conclusion:

Based upon the results obtained, the test material, Varisoft 222-90 Lot #SC49-68 644750, is considered a skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

Test Compound - Varisaf + 222-90
 pH Result LOT = SC49-0864750
NA
 Date Animals Received 4/10/81
 Date of Intradermal Injections 4/27/81
 Date of Topical Application 5/4/81
 Date of Challenge 5/18/81

RT No. 850040
 Sponsor No. NA
 Source Dear Paul
 Technician LJD, SW, TP
 Technician TP, NLD
 Technician NLD ER

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6410- 0236 ♂	0	/	0	/
0237 ♂	FOUND DEAD 5/9/81 ER		NA	
0238 ♂	0		0	
0239 ♂	1		0	
0240 ♂	0		0	
0241 ♂	0		0	
0242 ♂	3		2	
0243 ♂	1		0	
0244 ♂	0		0	
0245 ♂	0		0	
Technician	CO		JP	
Recorded By	ER		JP	
Date	1981 5/20		5/21	

NA - Not Applicable 5/18/81 NLD

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: NLD DATE: 5/29/81

① Maximization
Dermal Sensitisation In Guinea Pigs - Body Weights



Test Group RT No. 856940 Vehicle NA Test Compound Varisoft 222



Positive Control Group NA Vehicle NA

Lot # 5C49-68
644750

Animal Number								Technician	Date 1981
6410-0236	6410-0237	6410-0238	6410-0239	6410-0240	6410-0241	6410-0242	6410-0243		
451	500	449	478	449	398	426	463	SW	4/27
482	544	517	546	480	436	448	526	YYP	5/4
521	Found DEAD 5/9/81	544	577	483	441	453	584	JRYP	5/11
612		633	642	573	540	528	606	JRYP	5/18

		Animal Number	Tech- nician	Date
6410- 0244	6410- 0245			
424	427	Scale Used: K-Tron 4809	SW	4/27
462	463	Scale Used: K TRON 4809	YYP	5/4
446	463	Scale Used: K-Tron 4809	JRYP	5/11
531	552	Scale Used: K-Tron 4809	JRYP	5/18
		Scale Used:		
		Scale Used:		

① Form Change SW 4/27/81

NA - Not Applicable

Head
 (C) (S)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856940

Vehicle Sterile 0.9%

Test

Material Vorisor 222-9

Saline LOT # SC 49-68644750

Date Animal Received 4/13/81

Source Dean Paul Sex ♂

Date Initiated 4/23/81

Animal No. SITE	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0191 (2)	0.5	NA	NA	NA	NDJ	ER	4/23
		24	0	0	JP	JP	4/24
		48	0	0	MR	MR	4/25
0191 (2)	0.5	NA	NA	NA	NDJ	ER	4/23
		24	0	0	JP	JP	4/24
		48	0	0	MR	MR	4/25
0191 (C)	0.5	NA	NA	NA	NDJ	ER	4/23
		24	1.0	0	JP	JP	4/24
		48	1.0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No.

856940

Vehicle

Sterile 0.9%

Test

Material

Varisof 222-9

Saline

LOT # SC 49-68644

Date Animal Received

4/23/81

Source

Dean Daul

Sex

♂

Date Initiated

4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0130 A	0.5	NA	NA	NA	NDJ	ER	4/23
		24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
0130 B	0.5	NA	NA	NA	NDJ	ER	4/23
		24	0	0	JR	JR	4/24
		48	0	0	MR	MR	4/25
0130 C	0.5	NA	NA	NA	NDJ	ER	4/23
		24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856940

Vehicle Sterile 0.9%
Saline

Test

Material Varisof + 222-90
LOT # SC 49-686-175

Date Animal Received

4/13/81

Source

Dean Paul

Sex

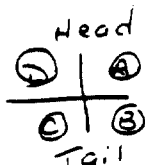
♂

Date Initiated

4/13/81

Animal No. <u>Site</u>	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0193 A	0.5	NA	NA	NA	NDJ	ER	4/23
	5.0%	24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
0193 B	0.5	NA	NA	NA	NDJ	ER	4/23
	10.0%	24	1.0	1.0	JR	JR	4/24
		48	1.0	1.0	MR	MR	4/25
0193 C	0.5	NA	NA	NA	NDJ	ER	4/23
	1.0%	24	0	0	JR	JR	4/24
		48	0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8516940

Vehicle Sterile 0.9% Saline

Test

Material Varisof 222-0
LOT # SC 49-68644750

Date Animal Received 4/3/81

Source Dean Dawl

Sex ♂

Date Initiated 4/21/81

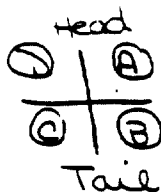
Animal No. <u>Site</u>	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0210 00120 (A)	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	2.0	1.0	CO	NDX	4/22
		48	2.0 3.0	3.0	JR	JR	4/23
0210 00120 (B)	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0210 00120 (C)	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0210 00120 (D)	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① Correction of error
CO 4/22/81

② Recording error JR 4/23/81



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☐

Test Group:

RT No. 856940

Vehicle sterile 0.9% Saline

Test

Material Varisof + 222-90
LOT # SC 49-68 644730

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0167 ②	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0167 ③	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	2.0	1.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0167 ④	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0167 ⑤	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

① Tail Head
② / ③
④ / ⑤
Tail -

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856940

Vehicle Sterile 0.9% Saline

Test

Material Varisort 222-90
LOT # SC 49-68644750

Date Animal Received

4/23/81

Source

Dean Daul

Sex

♂

Date Initiated

4/21/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
0145	0.5	NA	NA	NA	NDX	FR	1981 4/21
②	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0145	0.5	NA	NA	NA	NDX	FR	4/21
③	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0145	0.5	NA	NA	NA	NDX	FR	4/21
④	25%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0145	0.5	NA	NA	NA	NDX	FR	4/21
⑤	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
		NA	NA	NA			
		24					
		48					

① Recording Error 4/21/81 NDX

a - Dosage applied by technician indicated
NA - Not Applicable

Head
 ② | ①
 ③ | ④

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 85169-40

Vehicle Sterile 0.9% Saline

Test

Material Varisart 222-90
 LOT # SC49-68644750

Date Animal Received

4/3/81

Source

Dean Daul

Sex

♂

Date Initiated

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0169 A	0.5	NA	NA	NA	NDV	ER	4/21
	50%	24	2.0	2.0	CS	NDV	4/22
		48	3.0	3.0	JP	JP	4/23
0169 B	0.5	NA	NA	NA	NDV	ER	4/21
	75%	24	2.0	3.0	CS	NDV	4/22
		48	3.0	3.0	JP	JP	4/23
0169 C	0.5	NA	NA	NA	NDV	ER	4/21
	100%	24	2.0	3.0	CS	NDV	4/22
		48	3.0	3.0	JP	JP	4/23
0169 D	0.5	NA	NA	NA	NDV	ER	4/21
	25%	24	2.0	1.0	CS	NDV	4/22
		48	2.0	2.0	JP	JP	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head
 (C) (S)
 Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8516940

Vehicle Sterile 0.9%

Test

Material Vari. soft 222.9
Saline LOT # SC 49-68644750

Date Animal Received

4/13/81

Source

Dean's Paul

Sex

♂

Date Initiated

4/23/81

Animal No. SITE	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0191 (2)	0.5	NA	NA	NA	NJD	ER	4/23
	1.07%	24	0	0	JR	JR	4/24
		48	0	0	MR	MR	4/25
0191 (3)	0.5	NA	NA	NA	NJD	ER	4/23
	5.07%	24	0	0	JR	JR	4/24
		48	0	0	MR	MR	4/25
0191 (C)	0.5	NA	NA	NA	NJD	ER	4/23
	10.07%	24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856940

Vehicle Sterile 0.9%

Test

Material

Varisof 222-9
Saline LOT # SC 49-6864

Date Animal Received

4/13/81

Source

Dean Dawl

Sex

♂

Date Initiated

4/23/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0130 A	0.5	NA	NA	NA	NDJ	ER	4/23
	10.0%	24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
0130 B	0.5	NA	NA	NA	NDJ	ER	4/23
	1.0%	24	0	0	JR	JR	4/24
		48	0	0	MR	MR	4/25
0130 C	0.5	NA	NA	NA	NDJ	ER	4/23
	5.0%	24	1.0	0	JR	JR	4/24
		48	1.0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 851940

Vehicle Sterile 0.9% Saline

Test

Material Varisof + 222-90

LOT # SC 49-6864475

Date Animal Received

4/13/81

Source

Dean Paul

Sex

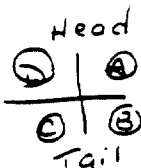
♂

Date Initiated

4/13/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410- <u>Site</u>							1981
0193 A	0.5	NA	NA	NA	NDJ	ER	4/23
	5.0%	24	1.0	0	JP	JP	4/24
		48	1.0	0	MR	MR	4/25
0193 B	0.5	NA	NA	NA	NDJ	ER	4/23
	10.0%	24	1.0	1.0	JP	JP	4/24
		48	1.0	1.0	MR	MR	4/25
0193 C	0.5	NA	NA	NA	NDJ	ER	4/23
	1.0%	24	0	0	R	R	4/24
		48	0	0	MR	MR	4/25
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 8516940

Vehicle Stenle 0.9%

Test

Material Varisof + 222-9

Saline

LOT # SC 49-68644730

Date Animal Received 4/3/81

Source Dean Dawl

Sex ♂

Date Initiated 4/21/81

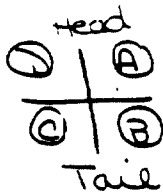
Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
							1981
0210 00120 ②	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	2.0	1.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0210 00120 ③	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0210 00120 ④	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0210 00120 ⑤	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

① Correction of Error
CO 4/22/81

② Recording error JR 4/23/81



Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☐ Test Group: RT No. 856940 Vehicle Sterile 0.9% Saline Test Material Varisof + 222-90 LOT # SC 49-68 644730

Date Animal Received 4/3/81

Source Dean Daul Sex ♂

Date Initiated 4/21/81

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
0167 ①	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0167 ②	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	2.0	1.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0167 ③	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
0167 ④	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JR	JR	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

① Head
②
③
④ Tail

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 856940

Vehicle Sterile 0.9% Saline

Test

Material Varisort 222-90

LOT # SC 49-68644750

Date Animal Received

4/13/81

Source

Debn Doul

Sex

♂

Date Initiated

4/21/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
0145 ①	0.5	NA	NA	NA	NDX	ER	4/21
	75%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0145 ②	0.5	NA	NA	NA	NDX	ER	4/21
	100%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0145 ③	0.5	NA	NA	NA	NDX	ER	4/21
	25%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
0145 ④	0.5	NA	NA	NA	NDX	ER	4/21
	50%	24	2.0	2.0	CO	NDX	4/22
		48	3.0	3.0	JP	JP	4/23
		NA	NA	NA			
		24					
		48					

① Recording Error 4/21/81 NDX

a - Dosage applied by technician indicated

NA - Not Applicable

Head
 (A) | (B)

 (C) | (D)

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

☒ Test Group: RT No. 8516940 Vehicle Sterile 0.9% Saline Test Material Varisoft 222-90 LOT # SC49-68644750

Date Animal Received 4/3/81

Source Dedn Daul Sex ♂

Date Initiated _____

Animal No. Site	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0169 (A)	0.5	NA	NA	NA	NDN	ER	4/21
	50%	24	2.0	2.0	CO	NDN	4/22
		48	3.0	3.0	JP	JP	4/23
0169 (B)	0.5	NA	NA	NA	NDN	ER	4/21
	75%	24	2.0	3.0	CO	NDN	4/22
		48	3.0	3.0	JP	JP	4/23
0169 (C)	0.5	NA	NA	NA	NDN	ER	4/21
	100%	24	2.0	3.0	CO	NDN	4/22
		48	3.0	3.0	JP	JP	4/23
0169 (D)	0.5	NA	NA	NA	NDN	ER	4/21
	25%	24	2.0	1.0	CO	NDN	4/22
		48	2.0	2.0	JP	JP	4/23
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
 NA - Not Applicable

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90
LOT 1183-K 184-857

SPONSOR: SHEREX CHEMICAL CO.
DUBLIN, OHIO

STUDY NO. 877521
INITIATION: 8/6/81
COMPLETION: 8/30/81
REPORTED: 9/15/81

SAMPLE: VARISOFT 222-90 LOT 1183-K 184-857

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED: Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot 1183-K 184-857

Test Animal: Young adult male guinea pigs were procured, maintained individually in galvanized steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 356 and 430 grams were chosen at random, and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 ml of sterile water for injection (in 1.0 ml increments) to 5.0 ml of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot 1183-K 184-857 and adding sterile water for injection to a total volume of 5.0 ml.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot 1183-K 184-857 in 2.5 ml of sterile water and adding 2.5 ml of Freund's Adjuvant (in 1.0 ml increments) to a total volume of 5.0 ml

For the topical induction the Varisoft 222-90 Lot 1183-K 184-857 was dosed at a 20% w/v mixture in sterile 0.9% saline. For the challenge application the Varisoft 222-90 was dosed at a 0.1% w/v mixture in sterile 0.9% saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material in Freund's Adjuvant.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 20% w/v mixture of Varisoft 222-90 in sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 0.1% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

RT LAB NUMBER 877521
GUINEA PIG MAXIMIZATION

PAGE 4

Test Animal: Albino guinea pigs
Source: Dean Daul, Luxemburg, WI
Date Animals Received: 7/29/81

Test Material: Varisoft 222-90 Lot 1183-K 184-857

Date Test Started: 8/6/81

Date Test Completed: 8/30/81

<u>Animal Number</u>	<u>Sex</u>	<u>24 Hours Right</u>	<u>48 Hours Right</u>
64100448	M	0	0
64100449	M	0	0
64100450	M	0	0
64100451	M	0	0
64100452	M	0	0
64100453	M	0	0
64100454	M	0	0
64100455	M	0	1.0
64100456	M	0	0
64100457	M	0	0

General Behavior and Appearance:

All of the guinea pigs used in this study appeared normal throughout the study period. Normal body weight gains were recorded for all animals during the course of the study, with the exception of one animal (No. 64100450) that exhibited a slight weight loss during the second week on test.

Skin Reactions to Varisoft 222-90: Lot 1183-K 184-857

One animal (No. 64100455) reacted to the challenge dose with a mild redness at the 48 hour observation. Nine animals did not exhibit any reaction to the challenge application at either the 24 or 48 hour observations.

Conclusions:

This test material is not considered a strong skin sensitizer in guinea pigs.

Reference:

Magnusson, B. MD, and A. Kligman, PhD, MD, Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-90: Lot 1183-K 184-857 RT No. 877521
 pH Result NA Sponsor No. NA
 Date Animals Received 7/29/81 Source Dean Daul
 Date of Intradermal Injections 8/12/81 Technician ER
 Date of Topical Application 8/13/81 Technician ER
 Date of Challenge 8/27/81 Technician ER

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
64/0- 0448 ♂	0		0	
0449 ♂	0		0	
0450 ♂	0		0	
0451 ♂	0		0	
0452 ♂	0		0	
0453 ♂	0		0	
0454 ♂	0		0	
0455 ♂	0		1.0	
0456 ♂	0		0	
0457 ♂	0		0	
Technician	ER		MP	
Recorded By	MP		ER	
Date 7/981	8/29		8/30	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: ER DATE: 9/4/81

Dermal Sensitization In Guinea Pigs - Body Weights

Varisoft 222-90



Test Group RT No. 877521 Vehicle NA Test Compound Lot 1183-K 184-89



Positive Control Group NA Vehicle NA

Animal Number								Technician	Date
6410-0448	6410-0449	6410-0450	6410-0451	6410-0452	6410-0453	6410-0454	6410-0455		
411	389	407	427	421	388	401	430	ER	8/6
460	449	461	506	485	432	444	485	ER	8/13
479	467	458	526	503	452	456	500	dw	8/20
584	556	545	564	552	515	534	586	SR	8/27

		Animal Number		
6410-0456	6410-0457		Tech-nician	Date 1981
413	356	Scale Used: K-Tron 4809	ER	8/6
462	410	Scale Used: K-Tron 4809	ER	8/13
478	440	Scale Used: K-Tron 4809	dw	8/20
558	501	Scale Used: K-Tron 4809	SR	8/27
		Scale Used:		
		Scale Used:		

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

Varisoft 222-90:

☒ Test Group RT No. 87752 Vehicle NA Test Compound Lot 1183-K 184-857

☐ Positive Control Group NA Vehicle NA Room No. 3

Animal Number								Tech- nician	Date 1981
6410- 0448	6410- 0449	6410- 0450	6410- 0451	6410- 0452	6410- 0453	6410- 0454	6410- 0455		
N	N	N	N	N	N	N	N	ND	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	ER	8/8
N	N	N	N	N	N	N	N	ME	8/9
N	N	N	N	N	N	N	N	dw	8/10
N	N	N	N	N	N	N	N	IR	8/11
N	N	N	N	N	N	N	N	Sh	8/12
N	N	N	N	N	N	N	N	ER	8/13
N	N	N	N	N	N	N	N	ER	8/14
N	N	N	N	N	N	N	N	IR	8/15
N	N	N	N	N	N	N	N	IR	8/16
N	N	N	N	N	N	N	N	dw	8/17
N	N	N	N	N	N	N	N	IR	8/18
N	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	ER	8/20
N	N	N	N	N	N	N	N	dw	8/21
N	N	N	N	N	N	N	N	ND	8/22
N	N	N	N	N	N	N	N	ND	8/23

N - No Visible Abnormalities

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

Varisoft 222-90:

☒ Test Group RT No. 877521 Vehicle NA Test Compound Lot 1183-K 184-857

☐ Positive Control Group NA Vehicle NA Room No. 3

Animal Number								Tech- nician	Date 1981
6410- 0456	6410- 0457								
N	N							NJD	8/10
N	N							ER	8/7
N	N							ER	8/8
N	N							MR	8/9
N	N							AW	8/10
N	N							JK	8/11
N	N							DA	8/12
N	N							ER	8/13
N	N							ER	8/14
N	N							JK	8/15
N	N							JK	8/16
N	N							AW	8/17
N	N							JK	8/18
N	N							ER	8/19
N	N							ER	8/20
N	N							AW	8/21
N	N							NJD	8/22
N	N							NJD	8/23

N - No Visible Abnormalities

NA - Not Applicable

Varisoft 222-90:

Positive Control Group NA Vehicle NA Room No. 3

NA - Not Applicable

Varisoft 222-90:

Positive Control Group NA Vehicle NA Room No. 3

N - No Visible Abnormalities

NA - Not Applicable

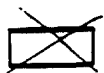
Head

A/B

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90



Test Group:

RT No. 877521 Sterile

Test

Vehicle 0.9% saline Material Lot 1183-K 184-8
Lot #23-712-DM-02

Date Animal Received 7/29/81

Source Deane Daul Sex ♀

Date Initiated 8/20/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
6410-0478	0.1%	NA	NA	NA	ER	ER	8/20
		24	0	0	ER	dw	8/21
		48	0	0	UN	UN	8/22
6410-0478	0.1%	NA	NA	NA	ER	ER	8/20
		24	0	0	ER	dw	8/21
		48	0	0	UN	UN	8/22
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Head

A/B
C/D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90

Sterile

Test



Test Group:

RT No. 877521

Vehicle 0.9% saline

Material

Lot 1183-K 184-8

Date Animal Received

7/10/81

Source Dean Daul

Sex

♀

Date Initiated

8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0417	1.0%	NA	NA	NA	ER	ER	8/7
		24	0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
0417	10%	NA	NA	NA	ER	ER	8/7
		24	0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
0417	20%	NA	NA	NA	ER	ER	8/7
		24	1.5	1.0	MR	MR	8/8
		48	2.0	1.0	MR	MR	8/9
0417	50%	NA	NA	NA	ER	ER	8/7
		24	3.0	2.0	MR	MR	8/8
		48	3.0	2.5	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head

A/B
C/D

Dose RangeDERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-907



Test Group:

RT No.

877521

Sterile

Test

Vehicle 0.9% saline

Material Lot 1183-K 184-857

Date Animal Received

7/10/81

Source

Dean Daul

Sex

♂

Date Initiated

8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date 1981
0381	10%	NA	NA	NA	ER	ER	8/7
		24	1.0	0	NR	NR	8/8
		48	0	0	NR	NR	8/9
0381	20%	NA	NA	NA	ER	ER	8/7
		24	1.5	1.5	NR	NR	8/8
		48	1.0	1.0	NR	NR	8/9
0381	50%	NA	NA	NA	ER	ER	8/7
		24	2.5	3.0	NR	NR	8/8
		48	1.5	2.0	NR	NR	8/9
0381	1.0%	NA	NA	NA	ER	ER	8/7
		24	2.0	2.0	NR	NR	8/8
		48	1.5	1.0	NR	NR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head

A/B
- C/D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90



Test Group:

RT No. 877521 Sterile Test

Vehicle 0.9% Saline Material Lot 1183K 184-85

Date Animal Received 7/10/81

Source Dean Paul Sex ♂

Date Initiated 8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
386	20%	NA	NA	NA	ER	ER	8/7
		24	1.0	1.0	MR	MR	8/8
		48	1.0	0	MR	MR	8/9
386	50%	NA	NA	NA	ER	ER	8/7
		24	3.0	2.5	MR	MR	8/8
		48	2.5	2.0	MR	MR	8/9
386	1.0%	NA	NA	NA	ER	ER	8/7
		24	0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
386	10%	NA	NA	NA	ER	ER	8/7
		24	1.0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90:

Sup: RT No. 877521 Vehicle sterile 0.9% saline Test Material Lot 1183K 184-857

Sal Received 7/10/81

Van Daul Sex ♂

Date Initiated 8/7/81

Dose ² (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
						1981
50%	NA	NA	NA	EP	EP	8/7
	24	3.0	2.0	MR	MR	8/8
0.5	48	3.0	2.5	MR	MR	8/9
1.0%	NA	NA	NA	EP	EP	8/7
	24	2.0	1.0	MR	MR	8/8
0.5	48	1.5	1.0	MR	MR	8/9
10%	NA	NA	NA	EP	EP	8/7
	24	1.0	0	MR	MR	8/8
0.5	48	1.0	0	MR	MR	8/9
20%	NA	NA	NA	EP	EP	8/7
	24	1.0	0	MR	MR	8/8
0.5	48	1.5	1.0	MR	MR	8/9
	NA	NA	NA			
	24					
	48					

e applied by technician-indicated
applicable

GUINEA PIG MAXIMIZATION STUDY OF VARISOFT 222-90
LOT 1184-K 184-857

SPONSOR: SHEREX CHEMICAL CO.
DUBLIN, OHIO

STUDY NO. 877522
INITIATION: 8/6/81
COMPLETION: 8/30/81
REPORTED: 9/15/81

SAMPLE: VARISOFT[®] 222-90 LOT 1184K 184-857

ENCLOSED: METHOD, PAGES 2 AND 3
SUMMARY, PAGE 4
RAW DATA APPENDIX

SIGNED:

Nancy J. Albrecht
NANCY J. ALBRECHT, BA
TECHNICAL SUPERVISOR

Gary W. Thompson
GARY W. THOMPSON, BS
MANAGER, ACUTE TOXICOLOGY
STUDY DIRECTOR

BY AND FOR RALTECH SCIENTIFIC SERVICES

RAW DATA FOR THIS STUDY IS KEPT ON FILE AT RALTECH SCIENTIFIC SERVICES,
MADISON, WISCONSIN.

Test Material: Varisoft 222-90 Lot 1184-K 184-857

Test Animal: Young adult male guinea pigs were procured, maintained individually in galvanized steel cages in temperature and humidity controlled rooms, provided continuous access to Purina Guinea Pig Chow and water and held for an acclimation period of at least 7 days.

Test System: Ten male guinea pigs weighing between 368 and 428 grams were chosen at random, and used for this study. The animals were individually housed and identified by animal number and ear tag.

Preparation of Test Material: For the intradermal injections the Freund's Complete Adjuvant Solution was prepared by adding 5.0 ml of sterile water for injection (in 1.0 ml increments) to 5.0 ml of Freund's Adjuvant.

The 5% solution of test material in sterile water was prepared by taking 0.25 gram of Varisoft 222-90 Lot 1184-K 184-857 and adding sterile water for injection to a total volume of 5.0 ml.

The 5% solution of test material in Freund's Adjuvant was prepared by dissolving 0.25 gram of Varisoft 222-90 Lot 1184-K 184-857 in 2.5 ml of sterile water and adding 2.5 ml of Freund's Adjuvant (in 1.0 ml increments) to a total volume of 5.0 ml

For the topical induction the Varisoft 222-90 Lot 1184-K 184-857 was dosed at a 20% w/v mixture in sterile 0.9% saline. For the challenge application the Varisoft 222-90 was dosed at a 0.1% w/v mixture in sterile 0.9% saline.

Method: A 4.0 x 6.0 cm area was clipped along the midline over the shoulder region. Two rows of three-deep intradermal injections (total of 6 injections) were made within the boundaries of a 2.0 x 4.0 cm area, one row on each side of the midline as follows: 0.05 ml of the prepared Freund's Adjuvant Solution, 0.05 ml of the 5% aqueous test solution, and 0.05 ml of the 5% solution of test material in Freund's Adjuvant.

One week after the injections, the same area was clipped and closely shaved with an electric razor. A 2.0 x 4.0 cm patch of Whatman No. 3 filter paper was saturated with a 20% w/v suspension of Varisoft 222-90 in sterile 0.9% saline, placed over the injection sites, then covered with an overlapping of Blenderm tape and secured by an overwrap of Elastoplast tape. The dressing remained in place for 48 hours.

Two weeks after topical induction the animals received a challenge dose. The hair was removed from a 5.0 x 5.0 cm area on the flank by clipping and

shaving as before. A 0.1% w/v suspension of test material in 0.9% saline was applied on a 2.0 x 2.0 cm piece of filter paper in the same fashion as for topical induction. The patch was sealed to the flank for 24 hours under a 4.0 cm strip of Blenderm tape. Complete occlusion was made by an overwrap with Elastoplast tape wound around the trunk.

Observations: Twenty-four hours following patch removal the test sites were examined for erythema and edema. The sites were examined again at 48 hours after patch removal to detect weak, slowly developing reactions. The test sites were shaved 3 hours prior to the 24 hour reading. The reactions were scored according to the following 4-point scale:

- 0 = no reaction
- 1 = scattered mild redness
- 2 = moderate and diffuse redness
- 3 = intense redness and swelling

The important statistic in maximization testing is the frequency of sensitization, not the intensity.

Test Animal: Albino guinea pigs
Source: Dean Daul, Luxemburg, WI
Date Animals Received: 7/29/81

Test Material: Varisoft 222-90 Lot 1184-K 184-857

Date Test Started: 8/6/81

Date Test Completed: 8/30/81

<u>Animal Number</u>	<u>Sex</u>	<u>24 Hours Right</u>	<u>48 Hours Right</u>
64100463	M	0	0
64100464	M	0	0
64100465	M	0	0
64100466	M	0	0
64100467	M	0	0
64100468	M	1.0	1.0
64100469	M	0	0
64100470	M	0	0
64100471	M	0	0
64100473	M	0	0

General Behavior and Appearance:

One animal (No. 64100463) exhibited diarrhea on study Days 9, 11, 12, and 13 and was observed with a red anal discharge on study Day 10. This animal was hypoactive and ataxic from Day 9 through Day 13 of the study. Another animal (No. 64100465) exhibited diarrhea on Day 23 of the study. Both of these animals appeared normal at all other observation periods. The remaining eight guinea pigs used in this study appeared normal throughout the study period.

With the exception of two animals (Nos. 64100463 and 64100466) that exhibited a loss in body weight and one animal (No. 64100465) that had a slight body weight gain at the end of the second week on test, normal body weight gains were recorded for all animals during the course of the study.

Skin Reactions to Varisoft 222-90: Lot 1184-K 184-857:

One animal (No. 64100468) reacted to the challenge dose with a mild redness at the 24 and 48 hour observations. Nine animals did not exhibit any reaction to the challenge application at either the 24 or 48 hour observations.

Conclusions:

This test material is not considered a strong skin sensitizer in guinea pigs.

Reference:

Mangusson, B. MD, and A. Kligman, PhD, MD. Allergic Contact Dermatitis in the Guinea Pig, Charles C. Thomas, pub., 1970, pp. 113-117.

GUINEA PIG MAXIMIZATION TEST

Test Compound Varisoft 222-90: Lot 1184-K 184-857 RT No. 877522

pH Result NA

Sponsor No. NA

Date Animals Received 7/29/81

Source Dean Daul

Date of Intradermal Injections 8/6/81

Technician JR

Date of Topical Application 8/13/81

Technician ER

Date of Challenge 8/27/81

Technician ER

Animal No., Sex	24 Hours		48 Hours	
	Right	Left	Right	Left
6410-0463 ♂	0		0	
0464 ♂	0		0	
0465 ♂	0		0	
0466 ♂	0		0	
0467 ♂	0		0	
0468 ♂	1.0		1.0	
0469 ♂	0		0	
0470 ♂	0		0	
0471 ♂	0		0	
0473 ♂	0		0	
Technician	ER		MP	
Recorded By	MP		ER	
Date	-1981 8/29		8/30	

Scoring Code: 0 = Normal, No Reaction
 1 = Scattered Mild Redness
 2 = Moderate and Diffuse Redness
 3 = Intense Redness and Swelling

REVIEWED BY: Sh DATE: 9/4/81

Dermal Sensitization In Guinea Pigs - Body Weights

Varisoft 222-9

☒ Test Group RT No. 877522 Vehicle NA Test Compound Lot 1184-K 184

☐ Positive Control Group NA Vehicle NA

Animal Number								Tech-nician	Date
6410-0463	6410-0464	6410-0465	6410-0466	6410-0467	6410-0468	6410-0469	6410-0470		
368	428	390	388	406	409	402	417	ER	8/6
437	491	466	447	460	474	475	481	ER	8/13
410	501	469	444	476	480	502	508	dw	8/20
482	606	578	533	552	581	587	592	JR	8/27

Animal Number			Tech-nician	Date
6410-0471	6410-0473			
403	404	Scale Used: K-Tron 4809	ER	8/6
458	467	Scale Used: K-Tron 4809	ER	8/13
492	486	Scale Used: K-Tron 4809	dw	8/20
589	577	Scale Used: K-Tron 4809	JR	8/27
		Scale Used:		
		Scale Used:		

NA - Not Applicable

Dermal Sensitization in Guinea Pigs - Daily Observations

☒ Test Group RT No. 877522 Vehicle NA Test Compound Varisoft 222-90:
☒ Positive Control Group NA Vehicle NA Room No. 3 Lot 1184-K 184-8

Animal Number								Technician	Date
6410-0463	6410-0464	6410-0465	6410-0466	6410-0467	6410-0468	6410-0469	6410-0470		
N	N	N	N	N	N	N	N	NR	8/6
N	N	N	N	N	N	N	N	ER	8/7
N	N	N	N	N	N	N	N	ER	8/8
N	N	N	N	N	N	N	N	NR	8/9
N	N	N	N	N	N	N	N	dw	8/10
N	N	N	N	N	N	N	N	JR	8/11
N	N	N	N	N	N	N	N	DR	8/12
N	N	N	N	N	N	N	N	ER	8/13
⊛ NA	N	N	N	N	N	N	N	ER	8/14
⊛ NA	N	N	N	N	N	N	N	DR	8/15
⊛ NA	N	N	N	N	N	N	N	JR	8/16
⊛ NA	N	N	N	N	N	N	N	dw	8/17
⊛ NA	N	N	N	N	N	N	N	JR	8/18
⊛ NA	N	N	N	N	N	N	N	ER	8/19
N	N	N	N	N	N	N	N	ER	8/20
N	N	N	N	N	N	N	N	ER	8/21
N	N	N	N	N	N	N	N	NR	8/22
N	N	N	N	N	N	N	N	NR	8/23

N - No Visible Abnormalities

NA - Not Applicable

⊛ animal has diarrhea and appears hypoactive and ataxia 8/14/81

⊛ animal has red anal discharge. APPEARS HYPOACTIVE & ATAXIC 8/15/81

⊛ animal appears hypoactive 8/19/81 ER

Dermal Sensitization in Guinea Pigs - Daily Observations Varisoft 222-90:

☒ Test Group RT No. 877522 Vehicle NA Test Compound Lot 1184-K 184-85

☐ Positive Control Group NA Vehicle NA Room No. 3

Animal Number								Technician	Date
6410-0471	6410-0473								
N	N							NDP	8/16/81
N	N							ER	8/7
N	N							ER	8/8
N	N							MR	8/9
N	N							MR	8/10
N	N							IR	8/11
N	N							Dh	8/12
N	N							ER	8/13
N	N							ER	8/14
N	N							IR	8/15
N	N							JK	8/16
N	N							daw	8/17
N	N							JR	8/18
N	N							ER	8/19
N	N							ER	8/20
N	N							ER	8/21
N	N							NDP	8/22
N	N							NDP	8/23

N - No Visible Abnormalities

NA - Not Applicable

Varisoft 222-90:

Varisoft 222-90:
Lot 1184-K 184-8

☒ Positive Control Group NA Vehicle NA Room No. 3

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

① animals had diarrhea 8/28/81 ER

② recording error 8/28/81 ER

Varisoft 222-90

☒ Test Group RT No. 877522 Vehicle NA Test Compound Lot 1184-K 184-8

NA Positive Control Group NA Vehicle NA Room No. 3

[illegible]

N - No Visible Abnormalities

NA - Not Applicable

① recording error 8/30/81 EL

Head

A | B

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-90



Test Group:

RT No.

877522

Vehicle sterile 0.9% saline

Test

Material Lot 1184-K 184-

Date Animal Received

7/29/81

Source

Dead Dawl

Sex

♂

Date Initiated

8/20/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded By	Date
6410-0489	0.1%	NA	NA	NA	EP	EP	8/20
	0.5	24	0	0	EP	da	8/21
		48	0	0	UN	UN	naa
6410-0489	0.1%	NA	NA	NA	EP	EP	8/20
	0.5	24	0	0	EP	da	8/21
		48	0	0	UN	UN	naa
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head
A/B
C/D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisof + 222-90

☒ Test Group: RT No. 877522 Vehicle saline, sterile Material Lot 1184-K 184-8

Date Animal Received 7/10/81

Source Dear Dawl Sex ♀

Date Initiated 8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date 1981
A 0444	1.0%	NA	NA	NA	EP	EP	8/7
	0.5	24	0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
B 0444	10.0%	NA	NA	NA	EP	EP	8/7
	0.5	24	1.5	1.0	MR	MR	8/8
		48	1.0	1.0	MR	MR	8/9
C 0444	20.0%	NA	NA	NA	EP	EP	8/7
	0.5	24	2.0	2.0	MR	MR	8/8
		48	2.0	1.5	MR	MR	8/9
D 0444	50.0%	NA	NA	NA	EP	EP	8/7
	0.5	24	2.0	1.0	MR	MR	8/8
		48	2.0	1.0	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head

A	B
C	D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 877522

Sterile

Test

Varisoft 222-90

Vehicle 0.9% saline

Material Lot 1184-K 184-85

Date Animal Received

7/10/81

Source

Dean Daul

Sex

♂

Date Initiated

8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0389	10%	NA	NA	NA	ER	ER	8/7
	0.5	24	1.0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
0389	20%	NA	NA	NA	ER	ER	8/7
	0.5	24	1.5	2.0	MR	MR	8/8
		48	1.0	1.0	MR	MR	8/9
0389	50%	NA	NA	NA	ER	ER	8/7
	0.5	24	2.5	3.0	MR	MR	8/8
		48	2.5	3.0	MR	MR	8/9
0389	1.0%	NA	NA	NA	ER	ER	8/7
	0.5	24	2.0	2.0	MR	MR	8/8
		48	2.0	1.0	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Head

A/B
C/D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS

Varisoft 222-



Test Group:

RT No. 877522

Sterile

Test

Vehicle 0.9% saline

Material Lot 1184-K 184-8

Date Animal Received

7/10/81

Source

Dean Daul

Sex

♂

Date Initiated

8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0343	20%	NA	NA	NA	SP	SP	8/7
		24	3.0	3.0	MR	MR	8/8
		48	3.5	3.0	MR	MR	8/9
0343	50%	NA	NA	NA	SP	SP	8/7
		24	2.5	2.0	MR	MR	8/8
		48	3.0	2.0	MR	MR	8/9
0343	1.0%	NA	NA	NA	SP	SP	8/7
		24	2.0	1.5	MR	MR	8/8
		48	2.0	1.0	MR	MR	8/9
0343	10%	NA	NA	NA	SP	SP	8/7
		24	1.0	1.0	MR	MR	8/8
		48	1.0	0	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated
NA - Not Applicable

Head

A	B
C	D

Dose Range

DERMAL SENSITIZATION STUDY IN GUINEA PIGS



Test Group:

RT No. 877522

Sterile

Test

Varisoft 222-90

Vehicle 0.9% saline

Material

Lt 1184-K 184-85

Date Animal Received

7/10/81

Source

Dean Dawl

Sex

♂

Date Initiated

8/7/81

Animal No.	Dose ^a (ml)	Observation Period (Hrs)	Erythema	Edema	Technician	Recorded by	Date
6410-							1981
0351	50%	NA	NA	NA	ER	ER	8/7
		24	1.0	1.5	MR	MR	8/8
		48	1.5	2.0	MR	MR	8/9
0351	1.0%	NA	NA	NA	ER	ER	8/7
		24	1.0	1.0	MR	MR	8/8
		48	0	0	MR	MR	8/9
0351	10%	NA	NA	NA	ER	ER	8/7
		24	0	0	MR	MR	8/8
		48	0	0	MR	MR	8/9
0351	20%	NA	NA	NA	ER	ER	8/7
		24	1.0	1.0	MR	MR	8/8
		48	1.5	1.0	MR	MR	8/9
		NA	NA	NA			
		24					
		48					

a - Dosage applied by technician indicated

NA - Not Applicable

Ethoxylated and Imidazolium Quaternary Ammonium Compounds:

Additional Information and Responses to letter dated
February 22, 1993 from Dr. John D. Walker,
Executive Director, TSCA Interagency Testing Committee,
to Dr. Jim T. Hill, Director PIR Program - CSMA in regard to
Data Submissions from QUATS Steering Committee Members
Filed in Response to the 22nd Report of the
TSCA Interagency Testing Committee

Attachment 21:

**Biodegradability, Varisoft 222
[PEQ 68410-69-5]**

3156

LABORATORY REPORT

Test: Biodegradability

Sample: Varisoft 222

Lab Data:

BOD₅ 408,000 mg/LBOD₂₀ 672,000 mg/LBOD₁₀ 532,000 mg/LBOD₃₀ 704,000 mg/L

COD (analytical) 2,290,800 mg/L

COD (theoretical) 2,230,750 mg/L

BOD₅/COD 0.18BOD₂₀/COD 0.29BOD₁₀/COD 0.23BOD₃₀/COD 0.31

Reaction Rate Constant 0.12

Results: Based on the above data, we feel Varisoft 222 can be considered biodegradable.

Analytical Procedures:

BOD: In determining the biodegradability of Varisoft 222, our laboratory conducted an Ultimate Oxygen Demand (UOD) study.

The product was aerated for eight (8) weeks with organisms supplied in settled raw sewage to acclimate them to this particular source of food. This was used as our seed material. In the UOD determinations, aliquots were incubated in the presence of the seed material at 20°C. Samples were taken ten (10) consecutive days and also after twenty (20) and thirty (30) days of incubation. BODs were determined on these samples (see attached analyses report), plotted against time and a reaction rate constant calculated.

COD: Chemical Oxygen Demand is determined by refluxing samples in 50% sulfuric acid solution with potassium dichromate which is the oxidizing agent. The amount of K₂Cr₂O₇ required to oxidize the sample is the COD.

Carl L. Andrews
Carl Andrews

Director of Laboratory

ANALYSIS REPORT

Des Plaines, Illinois

Date June 11, 1971

Unless otherwise noted - results in milligram per liter (mg/L)

Y: Carl L. Andrews

Director of Laboratory